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SCIENCE

4 August 1961
Vol. 134, No. 3475

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

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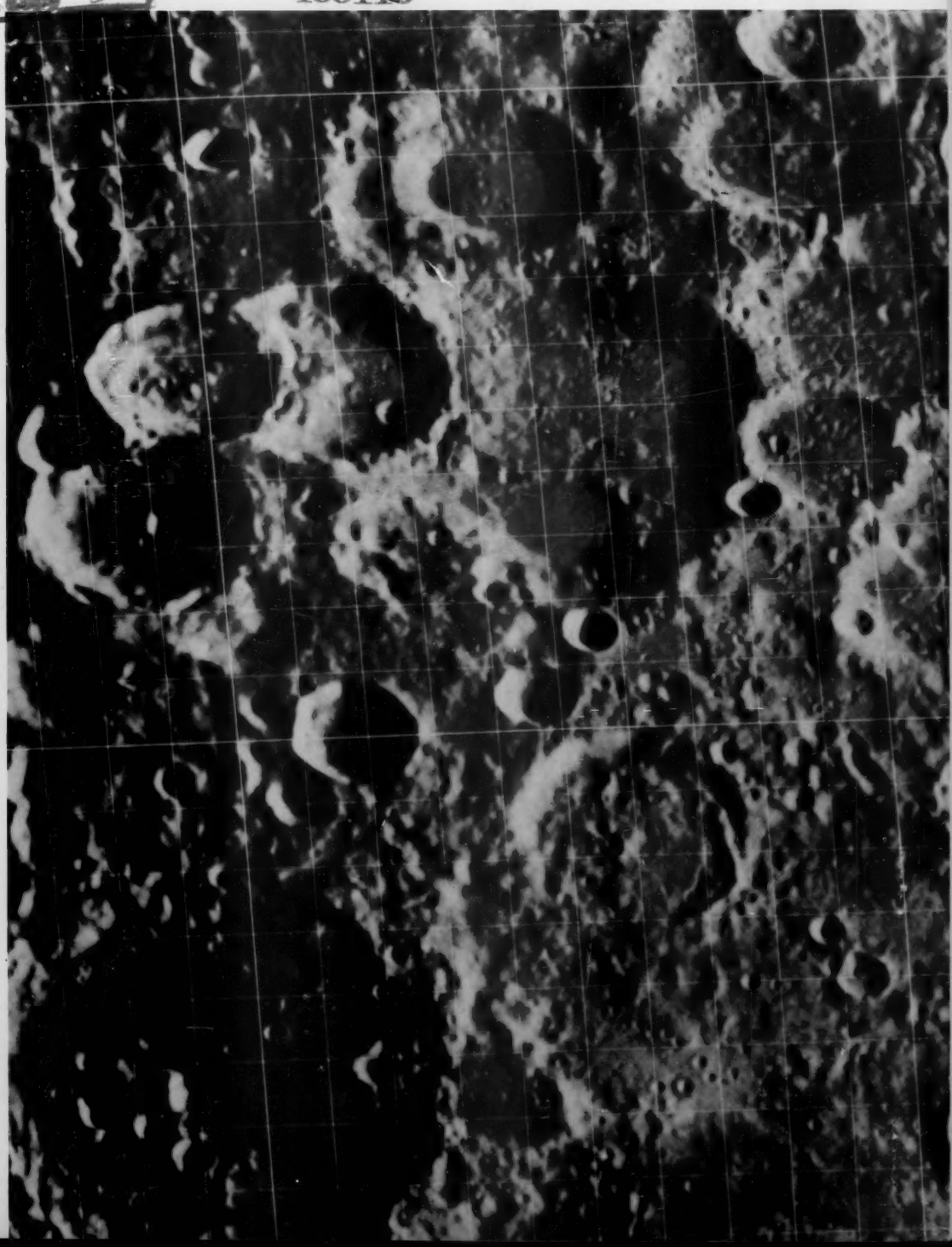

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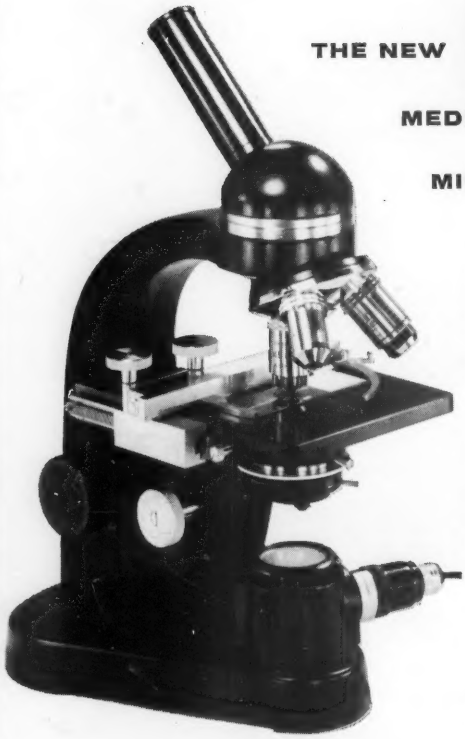

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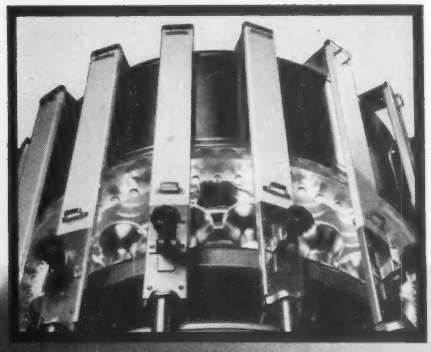

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Letters

Agricultural Aid to Underdeveloped Countries

It seems to me unfortunate that J. G. Harrar [*Science* **133**, 671 (1961)] concludes an excellent exposition of the role of research in promoting the 20th-century revolution in agriculture with a rather negative application to the underdeveloped countries of the world. He agrees that massive application of modern technologies could theoretically eliminate hunger, but he considers such application impossible in practice because of the lack of trained people to do the job. Education and training undoubtedly are necessary, and Harrar's words of caution are timely and well chosen. But must we wait until the gap is completely filled, and must the job necessarily be done on a massive scale?

Agricultural research in the United States began on a very modest scale and developed as the needs and opportunities became apparent. We now have extensive basic research and "highly sophisticated groups" of researchers because this early, relatively simple, inexpensive research was successful. Harrar probably would not characterize the Rockefeller agricultural improvement program in Mexico as massive, yet it has been eminently successful. A few years ago the United Nations, in cooperation with others, undertook to introduce hybrid corn into the corn-growing countries of Europe. Based on the concept of developing hybrids adapted to each country rather than on the use of United States hybrids, and directed by a modest amount of research, this effort also was highly successful, and relatively inexpensive.

Much of our current effort to improve agriculture in foreign countries consists of education of one kind or another, under the general heading of agricultural extension. Some of it has been less than conspicuously successful, not so much because it is not massive as because it has not been supported by research in the countries concerned. Most agricultural authorities agree that improved practices developed in the United States cannot safely and easily be transferred to other countries with different climates, soils, and economic conditions. Yet that is precisely what we have attempted to do in many cases, with nothing better to go on than experience in the United States. The result is suspicion and lack of confidence on the part of those we hope to help, and frustration on the part of those trying to do the job. One failure as a result of promoting an unsound or poorly adapted practice may offset the effect of a dozen successes. It seems to be but dimly realized that education, so far as it relates to agriculture, must be based, to be effective, on reliable, practical information of a sort that simply does not exist in most of these countries.

Agricultural research in the underdeveloped countries must, for the most part, be supported and conducted by the countries themselves. We can probably give most help by demonstrating the need for, and the value of, research, and by helping to train personnel to carry it out. Both efforts are essentially long-term rather than massive programs. Perhaps they should be patterned after similar programs in the United States, but above all they should be in accord with the capacity of the country concerned, and with the conditions that prevail in that country. What is needed, for the most part, is simple, well-planned experiments designed to solve the problems of immediate practical importance, conducted at enough places and for long enough periods to assure reasonably dependable results. So-called basic research can usually be deferred. Such practical research requires good over-all direction but not large numbers of highly trained people.

It is a strange fact that, although the need for an improved agriculture to alleviate hunger and to advance the economy in most underdeveloped countries is generally recognized, only a small proportion of foreign aid is devoted to either education or research in agriculture. The subject is sufficiently important to justify a positive rather than a negative approach.

S. C. SALMON

4103 Roanoke Road,
Hyattsville, Maryland

The editorial "Unhappy paradox" had such a familiar ring to it that I thought Harrar might be aware that I had written an article called "Paradox in paradise" for the *Journal of the American Institute of Architects* (September 1960).

The solution proposed by Harrar is in line with my own recommendations made after spending a year in an "underdeveloped area" as housing adviser to the government. However, I would like to suggest a different emphasis in the context of the educational process he advocates.

The peoples in the areas he has in mind are old culturally—much older and, in a sense, wiser than we are. They have, in common with all elderly people, a resentment of youth's temerity in assuming the role of teacher and the "mother knows best" attitude which our ICA missions are prone to maintain despite strong evidence that it won't work. Among other famous students of cultures, Margaret Mead has tacitly admitted that the problems associated with the paradox Harrar—and I—described cannot be readily resolved, and that the only attitude to be taken is one of patience (difficult in the face of Russian aggressiveness).

My own approach was based upon the sincere belief, acquired through being in the underdeveloped country for a few months, that the people there had much more to teach me than I had to teach them. I was then often able to offer the bits of technological information which might prove to be of some value. When the people wanted a college built I asked for instruction in *their* styles of building and *their* orientation for each of the buildings on an entire campus which I eventually was asked to design.

Peoples who have, for centuries, based their lives on human values we too often find only in textbooks or in a Sunday morning sermon cannot be convinced by precept that they "need" us or our knowledge. They can be forced to accept our bread and circus handouts, but the last ten years of American philanthropy seem to indicate that our approach is not amusing for very long.

I think one of our difficulties can be

Basic Research at Honeywell
Dr. Finn Larsen
Vice President for Research

Thermal Radiation: Studies In Emittance And Reflectance Properties of Materials

Because of possible high temperatures and the absence of an atmosphere, radiation becomes the primary method of heat transfer in space. Current interest in space exploration makes it mandatory to accurately determine the reflectance and emittance of various materials. Honeywell scientists have developed new techniques that promise useful new data on this method of heat transfer.

Heat transfer can take place in only three ways: convection currents, conduction, and radiation. Radiation becomes increasingly important to scientists because, at high temperatures or in a vacuum, it is the predominant or possibly the sole form of heat transfer. An understanding of radiation is particularly important today as man looks ahead to space travel. In space the vacuum exists, and high intensity heat radiation will be encountered.

In discussing heat transfer by radiation, clear terminology is important. Reflectance refers to that fraction of incident radiation that is reflected. The remaining fraction not reflected is absorbed when it strikes an opaque body. When given a numerical value it is called absorptance, and if the surface is at the same temperature as the radiator, absorptance is exactly equal to emittance. Emittance is the amount of energy emitted by a body related to the energy emitted by a perfect emitter given a value of unity. Thus, if reflectance (ρ) equals x, then absorptance (α) equals 1—x. And under conditions of temperature equilibrium, emittance (ϵ) also equals 1—x.

In transferring heat through radiation, the reflectance and emittance of surfaces determine the amount of heat transferred, and the understanding of emittance becomes the key to the heat transfer problems occurring in space.

Complicating our understanding of emittance is the fact that emittance is a function of the temperature of the surface under consideration. Also, emittance varies with the wave length of radiation.

The problem in the study of emittance over the years has been the inability to obtain consistent data. Various authorities have reported widely differing results. Contributing to these differing results is the inability to specifically describe identical surfaces and to repeat identical experimental conditions.

Additional problems complicating the ability to make comparable quantitative measurements are:

1) Energy from surrounding extraneous bodies is often reflected.
2) The measuring instrument cannot differentiate between reflected and emitted energy from the test specimen.
3) The amount of energy emitted varies with the angle of incidence with respect to the surface of the specimen.
4) Slight impurities can change the emittance characteristics of the specimen.
5) The atmosphere absorbs energy, thus the atmospheric pressure under which the observations are made is significant.

Honeywell scientists, however, have developed a new technique that avoids most of these problems. Their approach is to measure the spectral reflectance from which they can calculate spectral emittance. Total emittance and, therefore, total absorptance can be calculated by integrating spectral emittance.

Prior to the development of this technique, only a limited range of the spectrum could be measured by a single procedure. Different techniques and equipment were necessary to measure the remainder of the spectrum. The resulting multiplicity of procedures and equipment frequently introduced discrepancies.

With the Honeywell technique, monochromatic energy from an infra-red spectrometer is beamed on a diffuse reflector surface. The diffuse reflector is located at one of two conjugate foci of a highly reflecting integrating hemisphere. The energy is reflected by the diffuse reflector to the hemisphere. The hemisphere collects the energy and focuses it on the specimen located at the adjacent focus. Some of this energy is reflected out through a small port in the hemisphere to a sensor.

A complex equation involving the unknown reflectance and the known reflectance of a previously determined reference makes possible the calculation of the reflectance of the specimen.

It is possible to measure reflected energy in the presence of emitted energy, since all energy entering the system from the monochrometer is "chopped" at 13 cycles per second. Thus, energy reflected will also be at 13 cycles per second while inherently emitted energy will be continuous radiation.

Honeywell's apparatus and technique represents extensions of earlier work in the field. They are unique, however, in combining a monochromatic beam, an outside sensor, and a hemispheric reflector.

An important immediate result of the work done by Honeywell scientists is the ability to determine the specific emittance characteristics of different anodizing techniques for several different metals. Thus, accurate specification of an anodizing technique will predetermine the desired emittance. Ultimately it will permit specification of the entire surface of a space vehicle, allowing it to operate at predetermined temperature ranges in space. There are also several important industrial processes to which such knowledge would bring substantial improvement. Honeywell has as an eventual goal the control and adjustment of emittance in flight.

If you are engaged in scientific work relating to emittance and reflectance, and would like to know more about Honeywell's research, you are invited to correspond with Mr. J. E. Janssen, Honeywell Research Center, Hopkins, Minnesota. If you wish a recent paper by Mr. Janssen, write to Honeywell Research, Minneapolis 8, Minnesota.

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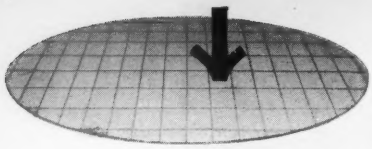

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traced not to the motives of the American people but to the motives of the people we send out to administer our foreign programs. We technicians may know how to work with people, but the administrators, mostly political appointees, know only how to work people in order that the sinecures garnered may be perpetuated. They survive chiefly because there are counterpart bureaucrats in the host country who have similar motives. The results are tragic both for the American taxpayer and for the natives he is trying to help. Another tragic consequence of the American political spoils system is the high regard native people begin to have for the Russian approach to their problems. This was described in the New York *Times* of 5 January 1960 by W. W. Kenworthy. He discussed the direct approach of setting up projects with specific objectives scaled to the understanding of the natives involved, as opposed to the grandiose million-dollars-be-damned approach of the Americans. The Russians try to impress the people affected; the Americans too often play to the politicians, whose prestige often depends upon how much they can squeeze out of Uncle Sam.

Instead of teaching people, I think we should merely allow them to learn at their own pace and in their own way. After all, as the people we want to help know so well, a way of life cannot be taught, it can only be lived.

MILTON D. LOWENSTEIN
Arizona State University, Tempe

Man on the Moon

It has, apparently, been decided that we shall be remembered as the only nation in history that felt that it could spare $9 billion—but could think of nothing better to do with it than to shoot it at the moon.

There has been remarkably little criticism of the proposal to put a man on the moon. Perhaps everyone is convinced that this is the supreme proof of our faith in science, and that it will be the final demonstration of our competence as scientists. It is not obvious, however, that science will, in the long run, benefit by being identified so closely with grandiose schemes whose real sponsors are the military hierarchy and the missile builders. Any layman or scientist should be able to name at least a hundred better ways to spend the money, and our more sophisticated friends abroad are apt to regard the project less as an affirmation of national determination than as a declaration of intellectual bankruptcy.

Just as a timid suggestion, why not have the AAAS sponsor a contest in which each bright young graduate would list the ten best ways to spend $1 billion.

WILLIAM PALMER TAYLOR
416 Ross Avenue,
Hamilton, Ohio

"Mad-Baiting"

The increasing interest in mental health these days seems to be associated with a rather significant, albeit comparatively unnoticed, political phenomenon—the phenomenon of "mad-baiting." There even seems to be some evidence of this phenomenon in the situation described in your "Mental health in the House Rules Committee" [*Science* **133**, 1468 (12 May 1961)], even though the conclusions are certainly sound.

In "mad-baiting," scientific evaluation of ideas, and of disturbing ideas in particular, is avoided by labeling their promulgators "mad" or "disturbed." Sometimes technical diagnosis, often from afar, lend a veneer of scientific credibility to such *ad hominem* attacks on ideas. Instead of being soberly examined, ideas of this sort are then either ignored or else fought with blind fury, as though the devil himself had created them. Which response actually occurs in a given situation is likely to be determined much more by unthinking, popular attitudes, often prejudicially shaped by the mass media, than by the nature of the ideas themselves.

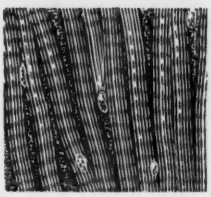
Scientific method demands, however, that ideas be carefully examined and soberly responded to on their own merits. Only after an individual's ideas have been repeatedly shown to be consistently wrong are we entitled to begin to question either his motives or his stability; even here, however, the term *sick* begs the basic question of whether the errors are accidental or, as with Adolph Hitler, deliberate lies.

Name-calling is an old political tactic. A new pseudoscientific veneer to either "mad-baiting" or "red-baiting" in these psychologically oriented days should not prevent us from recognizing its basically obfuscatory function, and its antidemocratic and antiscientific effect.

NATHANIEL S. LEHRMAN
15 Canterbury Road,
Great Neck, New York

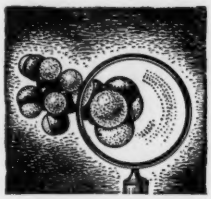
IT HAPPENED THIS MONTH...

a glance at yesterday in relation to today



IN AUGUST – (1798) – *Philosophical Magazine* speculates upon the nature of muscular contraction. "It appears very certain that the cause of muscular movement is owing to the nerves . . . But how does the nerve move? Some philosophers have compared its movement to the oscillation of an extended cord which is struck: But, 1. The nerves are not extended: 2. They are enveloped on all sides; whereas the cord has no points of contact but at its two extremities. It appears more probable to others to consider the nerve as . . . a series of vehicles in which flows a fluid called the nervous fluid. I have supposed that this nervous fluid is of a nature analagous to the *aura feminalis*. Others have fought for the cause of irritability in electricity, and the experiments in Galvanism seem to give some weight to this opinion."[1]

Now, a century and a half later, there are still many unanswered questions as to the nature of muscular contraction. There is general agreement, however, on the importance of ATP as the source of chemical energy for muscular movement. Schwarz has long played a leading role in providing ATP and other biochemical phosphates involved in energy transfer reactions – ADP, adenylic acid, adenosine-3′:5′-cyclic phosphate, GTP, GDP, CTP, and CDP. Some of these compounds are available in radiochemical form. In addition, we supply dehydrated firefly tails for precise and specific micro assay of ATP.



IN AUGUST – (1938) – a report from Paris provides insight into the role of sulfhydryl groups in enzymatic activity. It is suggested that changes in the activity of the enzymes may be attributed to oxidation and reduction of SH groups. Rapkine[2] has shown that oxidized glutathione inactivates the enzyme catalyzing the oxidation-reduction reaction between triosephosphate and pyruvate. If the excess glutathione is dialysed away, the enzyme can be reactivated by reduced glutathione or cysteine, the latter being more rapid in its action.

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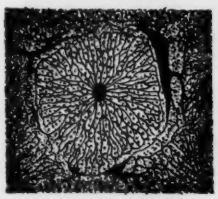

IN AUGUST – (1953) – a group of Scottish investigators[3] discusses the incorporation of N^{15}-glycine, C^{14}-formate, and S^{35}-methionine into the nucleic acids and proteins of rat liver cell nuclei and cytoplasmic fractions. Nuclear DNA incorporated C^{14} and N^{15} at a slow rate, but nuclear RNA showed greater activity than the RNA of mitochondria, microsomes, or cell sap. With all three isotopes there was no great difference between rate of incorporation into nuclear and into cytoplasmic protein. This indicates that nuclear RNA and protein play an active role in metabolic processes in non-dividing cells.

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1. Irritability of the animal fibre. Philosophical Magazine *1*:307 (Aug.) 1798. 2. Rapkine, L.: Sulphydryl groups and enzymic oxido-reduction. Biochem. J. *32*:1729, 1938. 3. Smellie, R. S.; McIndoe, W. M., and Davidson, J. N.: The incorporation of N^{15}, S^{35}, and C^{14} into nucleic acids and proteins of rat liver. Biochem. et Biophys. Acta *11*:559 (August) 1953.

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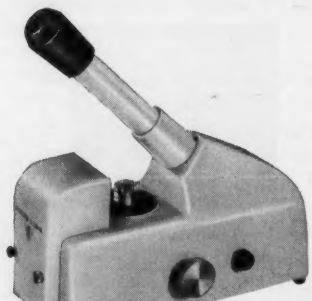

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SCIENCE, now combined with THE SCIENTIFIC MONTHLY, is published each Friday by the American Association for the Advancement of Science at National Publishing Company, Washington, D.C. SCIENCE is indexed in the *Reader's Guide to Periodical Literature.*

Editorial correspondence should be addressed to SCIENCE, 1515 Massachusetts Ave., NW, Washington 5, D.C. Manuscripts should be typed with double spacing and submitted in duplicate. The AAAS assumes no responsibility for the safety of manuscripts. Opinions expressed by authors are their own and do not necessarily reflect the opinions of the AAAS or the institutions with which the authors are affiliated. For detailed suggestions on the preparation of manuscripts, see *Science* **125**, 16 (4 Jan. 1957).

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Chinese Embargo

The newest volume in the AAAS symposium series is *Sciences in Communist China.* The volume and the symposium at the 1960 AAAS meeting at which the 26 papers were originally presented, some in shortened form, involved the cooperation of many people and organizations: a grant from the National Science Foundation, the joint planning of 10 scientific societies with the annual AAAS Conference on Scientific Communication, the scholarship of 30 authors, and the collection from many sources and the distribution to these authors of a quarter of a million pages of Chinese scientific literature of the past decade.

The result is a field-by-field summary that presents both some praiseworthy accomplishments and some failures to achieve the high hopes of Chinese government planners and scientific leaders. The symposium volume, the original literature (which is now on deposit at the Massachusetts Institute of Technology library), and the translations of a number of 10-year reviews written in Communist China by Chinese scholars, each summarizing advances of the past decade in a single field, make available a massive amount of material that hitherto has been scattered and, in the main, available only to persons who could read Chinese.

It is unlikely that there will be another such compilation in the near future, for the Chinese have virtually stopped exporting copies of their scientific journals. Only a trickle has come out since the end of 1959.

The embargo cuts both ways. It will be more difficult for the Western world to learn what is happening in the scientific institutions of Communist China. And it will be harder for Chinese scientists to keep up with Western literature since exchange arrangements have been cut off by the embargo. Clearly this means a loss to scientists in China. It also means some loss to scientists in other countries, and a loss, also, to that abstract entity science itself.

Commenting on the symposium presented in New York, the columnist Holmes Alexander—knowing that he was advocating an unpopular position—recommended continued isolation of Chinese scientists from the rest of the world because "as far down the road as anybody can see, our sworn enemies in Asia would have far more to gain from the exchange than we would." When there is free scientific communication across a border, the less advanced group stands a greater chance of learning something new than does the more advanced group. But the more advanced group has a greater capacity to utilize any new findings gleaned from the other's literature. Which loss is the greater might be debated, but for the moment let us agree with Mr. Alexander that the Chinese have more to gain from a free exchange than we do. Why, then, have they ceased to export their own literature?

A semiofficial explanation is that paper is in short supply and that the number of copies printed does not allow for export, but some skeptics suggest that the real reason is that Chinese science has not advanced as rapidly as their national leaders predicted and that the embargo is to prevent loss of face.

Whatever the reason, the decision was probably politically determined. It is, therefore, not likely to be changed until China learns, as, we hope, the U.S.S.R. and the Western nations have learned, that a nation that attempts to isolate itself from international scientific communication loses more than it gains.—D.W.

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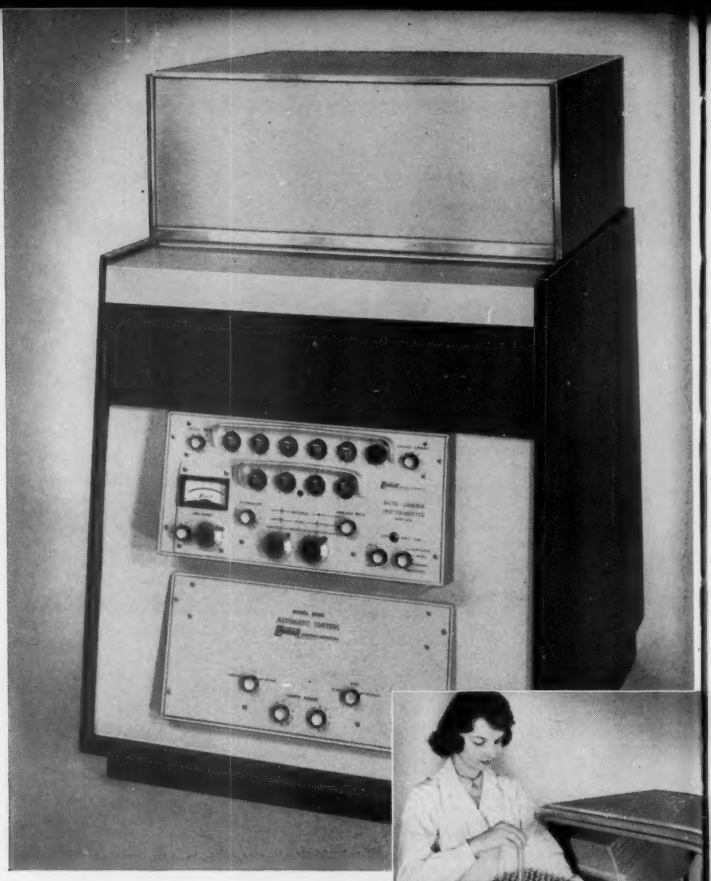

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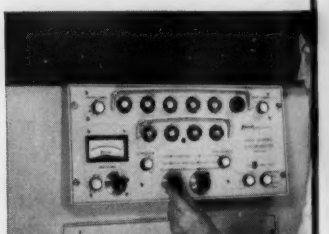

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4 August 1961, Volume 134, Number 3475 SCIENCE

CURRENT PROBLEMS IN RESEARCH

Chemistry of Lignification

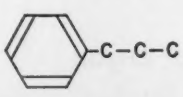
Biochemical research on lignins is yielding clues to the structure and formation of these complex polymers.

Stewart A. Brown

Nearly a century and a quarter has passed since Anselme Payen first used the term *lignin* in reference to the "incrusting material" which he removed from wood by the application of acidic and alkaline reagents. In the intervening years the advances in our knowledge of this complex material have been slow, often uncertain, and attended by considerable frustration. The difficulties involved have paralleled to some extent those encountered in the study of other natural polymers, but because of a unique combination of complicating factors the structure of lignin is even today far from being completely understood.

One such factor is the inhomogeneity of lignin, and it is worth while to point out at the beginning that the name in its singular form is a misnomer. Even if only simple polymers are considered, there are three different lignins, and if one accepts the existence of mixed polymers formed from more than one of the three known monomers, the number of potential lignins can be large indeed. Among other natural polymers it is possible that only proteins exceed lignin in complexity, but in one respect lignins have proved even more intractable than proteins, because no lignin has yet been obtained in crystalline form. The problem of purification has been a major impediment in determining the structure of lignin; different isolation procedures employed with the same starting material have yielded lignin preparations with appreciably different properties, so that lignin chemists have never been sure to what extent they have been working with artifacts. Still another complication has been the multiplicity of products, most of which have successfully resisted purification, that arise from degradative reactions. In spite of the great variety of attacks on the lignin polymer it has never proved possible, even with new techniques, to recover anything approaching quantitative yields of pure reaction products. Such pure products have been monomeric in nature, and the failure to recover oligomeric degradation products has severely handicapped efforts to find clues to the intramolecular linkages present in lignins.

Although there have been some dissenting opinions, there has been increasing acceptance in recent years of a concept of lignin proposed as long ago as 1897 by the Swedish chemist Klason—that of a polymer consisting predominantly, if not entirely, of phenylpropanoid (C_6, C_3) units:



I do not intend in this article to deal with the structural chemistry of lignin except as it relates directly to lignin formation in the plant. Readers interested in the structural chemistry of lignin, or in aspects of lignification other than chemical, are referred to several recent reviews dealing with these subjects (*1*, *2*).

Much speculation occurs in the older literature about the mode of lignin formation, but it has been only during the last decade or so that the availability of new weapons, such as radioactive tracers and refined chromatographic techniques, has made feasible a direct attack on the problem of biosynthesis. It is largely the research carried out during this period that I shall cover here. For a more comprehensive and detailed review of this field the recent treatise by Brauns and Brauns (*2*) is recommended.

Degradative Techniques

In most studies of biosynthesis involving tracers the product in question must be isolated from the organism and purified. Some attempts have been made to interpret the results of carbon-14 analyses on isolated lignins, but in general, because of purification difficulties, workers in this field have had recourse to chemical degradation for the recovery of certain monomeric products, which have known structures and can be purified with confidence. Three types of degradation have been most useful in this respect.

1) *Oxidation.* The use of nitrobenzene as an oxidant leads to the formation of the substituted benzaldehydes (see Fig. 1), vanillin (I), syringaldehyde (II), and *p*-hydroxybenzaldehyde (III). Spruce wood, which has been the most extensively studied, yields vanillin alone, in common with most other conifers (gymnosperms). The wood of deciduous trees (angiosperms) yields in addition syringaldehyde, and monocotyledons such as the grasses yield all three phenolic aldehydes, although much of the *p*-hydroxybenzaldehyde

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appears to originate from oxidation of the amino acid tyrosine if any protein is present (*3*). Another oxidant, permanganate, has been useful in forming benzenedicarboxylic acids which have given some important clues to the intramolecular linkages (*4*).

2) *Ethanolysis.* Prolonged heating of lignified material with ethanol containing hydrochloric acid produces small amounts of compounds, of which IV to VI (R = H or R = CH_3O) shown in Fig. 1 are predominant. These ethanolysis products are phenylpropanoid (C_6, C_3) compounds, and although they are recovered in a lower yield, their structural resemblance to the assumed lignin monomer gives them advantages over the oxidation products, which have lost two side-chain carbon atoms. Gymnosperm lignin yields compounds in which R = H, and from angiosperm lignin are recovered, in addition, compounds in which R = CH_3O (with *two* methoxyl groups).

3) *Hydrogenolysis.* The products VII (R = H or R = CH_3O) in Fig. 1 can be recovered in low yield after hydrogenolysis of lignified material over Raney nickel catalyst. Like the products of ethanolysis, they have the advantage of retaining all the carbon atoms of the phenylpropanoid skeleton.

Conversion of Carbon Dioxide to Lignin

In common with all other organic plant constituents lignin must be derived ultimately from carbon dioxide. In a discussion of its formation the most logical approach would probably be to trace the reactions by which carbon dioxide is converted to the lignin monomers, and finally to discuss the polymerization reactions by which lignin is finally synthesized. Historically, though, the problem has been attacked to some extent from the opposite direction, with the result that much was known about the polymerization before very extensive research had been done on the origin of the monomers. We examine the polymerization studies first, because this approach has the additional advantage of providing an insight into the nature of the lignin structures toward which the earlier metabolic reactions are directed.

Before proceeding with this I should like to mention some early studies in which the over-all transformation of carbon dioxide to lignin was investigated. Carbon dioxide labeled with carbon-14 has been of great value in the study of some aspects of plant metabolism, as witness the well-known work of Calvin's group on the path of carbon in photosynthesis. But its value tends to decrease in the study of plant constituents further removed from carbon dioxide, because in the longer times required for their synthesis, randomization of carbon-14 becomes extensive through the recycling of intermediates, and interpretation of the observed labeling becomes excessively difficult. But much information, especially that concerning time relationships, is obtainable through the use of C^{14}-labeled carbon dioxide.

Stone and his co-workers (*5*) used C^{14}-labeled carbon dioxide to study rates of lignin synthesis and possible breakdown in wheat plants. They exposed the plants to labeled carbon dioxide just before the beginning of rapid lignification, which had been shown to begin about 45 days after seeding, and at varying intervals thereafter determined the carbon-14 present in the phenolic aldehydes formed from lignin by oxidation. The results showed that the formation of lignin was a surprisingly slow process, not becoming rapid until 4 to 6 hours after activation. (The early products of photosynthesis acquire high activity from C^{14}-labeled carbon dioxide within seconds.) Over longer periods, although the total activity in the *tissues* as a whole declined gradually through respiration, the total activity in *lignin*, represented by phenolic aldehydes, remained substantially

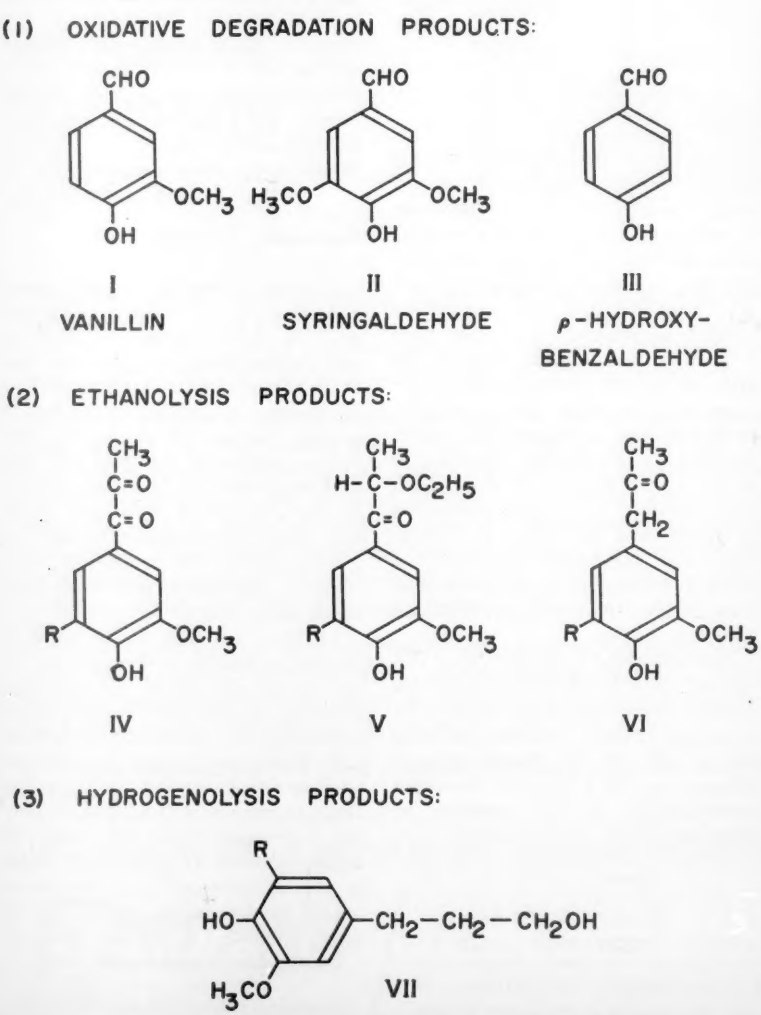


Fig. 1. Degradation products of lignins used in the study of lignification.

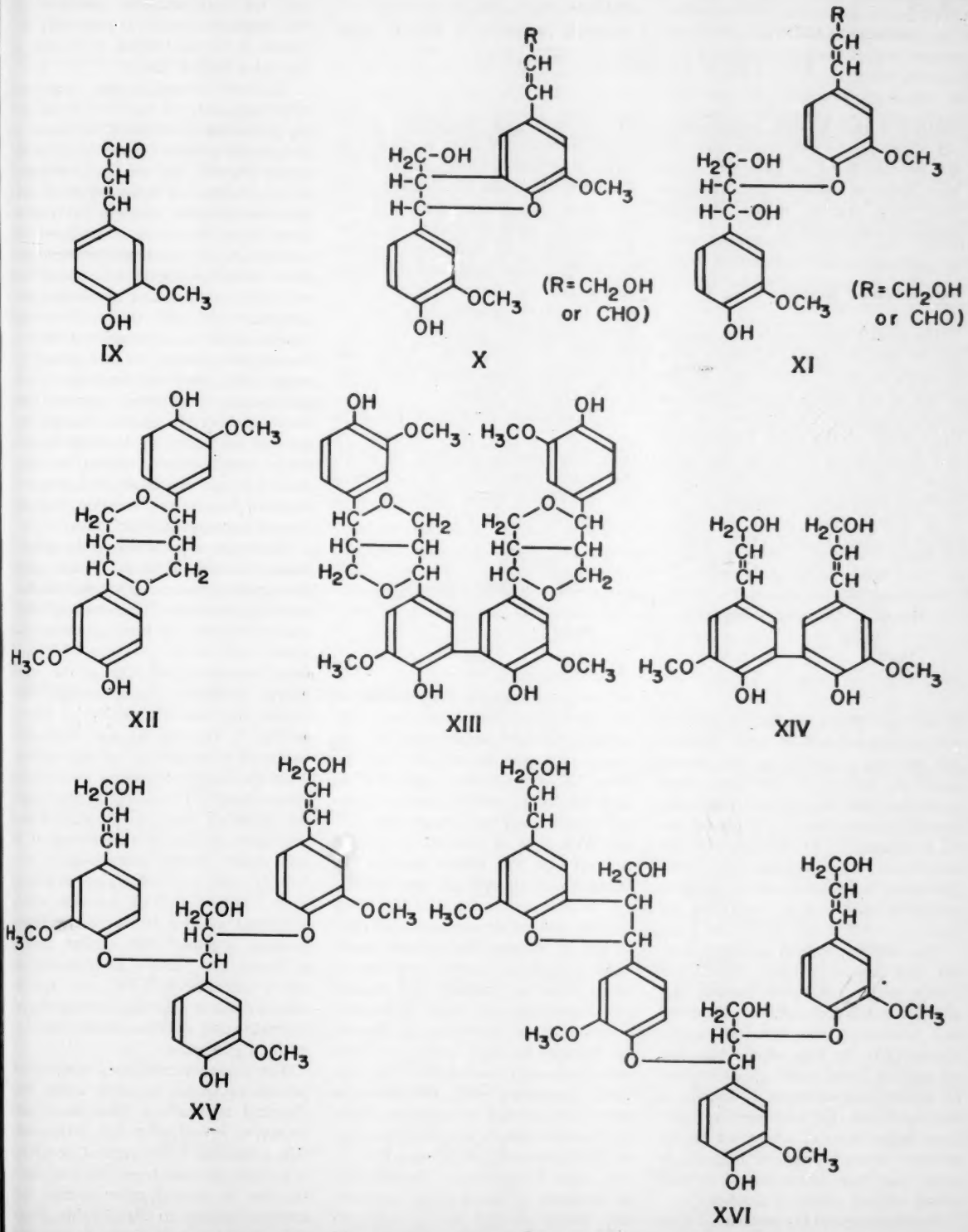


Fig. 2. Products of the action of mushroom laccase on coniferyl alcohol.

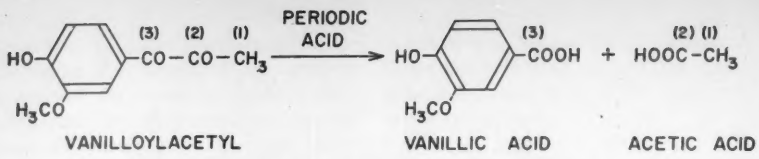
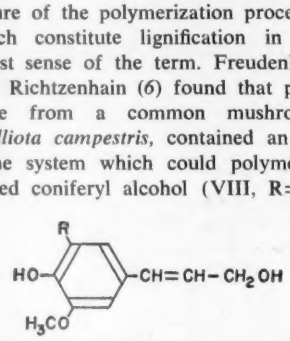


Fig. 3. Chemical degradation of vanilloylacetyl.

constant. Lignin is, then, an end product of the plant's metabolism and cannot be considered to have any metabolic function, once formed. Its functions seem, rather, to be primarily structural and protective.

Polymerization Reactions

The studies begun nearly two decades ago by Freudenberg in Germany have given us a much clearer idea of the nature of the polymerization processes which constitute lignification in the truest sense of the term. Freudenberg and Richtzenhain (*6*) found that press juice from a common mushroom, *Psalliota campestris*, contained an enzyme system which could polymerize added coniferyl alcohol (VIII, R=H)



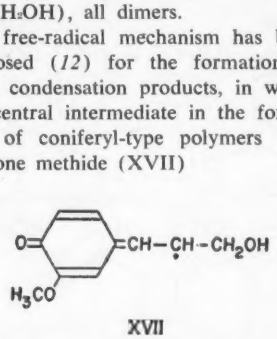
VIII

to an amorphous product bearing a striking resemblance in both chemical and physical properties to the natural lignin of conifers. It has since been established that the enzyme responsible for this polymerization is a phenol oxidase, laccase (*7, 8*), but it is still not completely clear whether the polymerization in higher plants is catalyzed chiefly by laccase or by peroxidase (*8, 9*).

The addition of both coniferyl alcohol and sinapyl alcohol (VIII, R= CH_3O) to the mushroom enzyme system led to the formation of a copolymer resembling the lignin of angiosperms (*10*). In view of the fact that no natural lignin made up exclusively of sinapyl alcohol units is known, it was significant that no lignin-like polymers higher than dimers could be recovered from a reaction mixture to which had been added sinapyl alcohol alone, without coniferyl alcohol.

Freudenberg and his associates found that if they interrupted the reaction at an early stage, a number of products of relatively low molecular weight could be recovered from reaction mixtures in which coniferyl alcohol was the substrate. Some 40 of these products have been distinguished, and with the aid of chromatography on cellulose columns, 11 have been purified (*11*). Structures published for these compounds are shown in Fig. 2. The most important quantitatively are dehydrodiconiferyl alcohol (X, R= CH_2OH), DL-pinoresinol (XII), and guaiacylglycerol-β-coniferyl ether (XI, R=CH_2OH), all dimers.

A free-radical mechanism has been proposed (*12*) for the formation of these condensation products, in which the central intermediate in the formation of coniferyl-type polymers is a quinone methide (XVII)



XVII

and some evidence for the existence of such an intermediate has been presented (*13*). In a similar way the formation of a quinone methide from the dimer XI, R = CH_2OH, could lead to molecules with a higher degree of polymerization, such as compounds XV and XVI. It is of interest, in view of the fact that this theory predicts the formation of an optically inactive lignin, that the intermediates of Fig. 2 are inactive, and no demonstration of optical activity in lignin has yet been made.

As pointed out earlier, attempts to isolate from the chemical and biological degradation of lignin oligomeric products which could provide clues to the linkages between monomers have been consistently unsuccessful. The synthetic approach of Freudenberg's group thus appears to represent a major breakthrough in our understanding of lignin structure. At present this applies only to coniferous lignins, and the structure of lignins which also contain sinapyl alcohol and possibly *p*-hydroxycinnamyl alcohol units is still little understood. Although it is true that the German workers have derived their enzyme system from a plant which does not normally lignify, there seems to be no good reason to believe that the polymerization catalyzed by the mushroom system is essentially different in its mechanism from that in lignifying higher plants.

Coniferyl alcohol is not known to occur naturally in the free form, but its β-glucoside, coniferin, is found in coniferous species. On the basis of experiments with the conifer *Araucaria*, Freudenberg *et al.* have suggested that the more soluble coniferin is translocated from its site of synthesis to the vicinity of the cambium, where coniferyl alcohol is liberated by the action of a β-glucosidase and then undergoes polymerization (*14*). Higuchi and his co-workers (*15*) were able to show a correlation between the rate of lignification and the concentration of β-glucosidase in different zones of the bamboo shoot. In general, though, the role of coniferin, at least in species other than conifers, cannot be considered to be fully established. Even in conifers its primary function may be that of a storage product.

More extensive studies on the utilization of coniferin in the intact plant have been carried out by Kratzl, Billek, and their associates. They used ethanolysis to degrade the lignin from spruce wood into which coniferin-3-C^{14} had been implanted (*16*). One of the ethanolysis products, vanilloylacetyl, was further degraded chemically, as shown in Fig. 3. The vanillic acid from this oxidation accounted for all the carbon-14 in the vanilloylacetyl, as would have been expected if coniferyl alcohol from the coniferin had been incorporated into lignin without rearrangement of its side chain. When coniferin-2-C^{14} was fed (*17*), the 2-carbon fragment arising from C-1 and C-2 of the side chain contained all the radioactivity. These findings, together with similar results of Brown and Neish (*18*) in studies in which cinnamic acid-3-C^{14} was fed to wheat, make it clear that no significant reconstruction of the side chain occurs during lignification.

Tissue-culture techniques, which have proved so useful in many other biochemical applications, have been used by several investigators (*19, 20*) to obtain additional evidence that coniferin is a lignin precursor, not only in conifers but in several other species not known normally to contain this glucoside. Peroxide was shown to enhance the polymerization, and substances

known to be peroxidase inhibitors were shown to inhibit it, providing further evidence that the polymerization is, at least in some tissues, mediated by peroxidase.

Pathway from Carbohydrates to Lignin Monomers

An equally important aspect of lignification concerns the biosynthetic route leading from carbon dioxide to the lignin monomer or monomers. It has long been assumed that lignin is synthesized, in common with other organic plant constituents, from carbohydrates formed in photosynthesis. But it has been only within the past decade that the pathways by which aromatic rings are formed have begun to be revealed in detail. The first clues to the reactions involved came not from higher plants but from the now well-known studies of Davis, Sprinson, and their associates on mutants of the bacterium *Escherichia coli* (*21*). These radiation-induced mutants, which lacked enzymes necessary for aromatic ring formation, accumulated in the growth-medium compounds which have proved to be obligatory intermediates in the conversion of sugars to benzenoid compounds. The pathway, as understood at present, is shown in Fig. 4. One of the cyclic pre-aromatic compounds is shikimic acid (XXIV), which is now known to accumulate in many plants. By condensation of shikimic acid phosphate (XXV) with phosphoenolpyruvic acid (XIX) there is formed prephenic acid (XXVII), which in turn reacts to form phenylpyruvic acid (XXVIII), the first fully aromatic compound synthesized. In an alternative pathway the hydroxyl group of prephenic acid is retained, and the product is *p*-hydroxyphenylpyruvic acid (XXIX) (*22*).

The fact that the first aromatic compounds resulting from the shikimic acid pathway were phenylpropanoid in nature, with a carbon skeleton resembling that of the cinnamyl alcohols, led Brown and Neish to suspect that the shikimic acid pathway might participate in lignification. It was demonstrated (*23*) that C^{14}-labeled shikimic acid and L-phenylalanine were incorporated into the lignin of wheat and maple with a quite low dilution of the carbon-14, whereas the dilution of carbon-14 from a C_6C_1 compound, 3,4-dihydroxybenzoic acid, whose ring substitution resembled that of coniferyl alcohol, was much greater, indicating much less efficient utilization. Eberhardt and Schubert (*24*) complemented this finding by showing that no rearrangement of carbon atoms took place during the conversion of radioactive shikimic acid to lignin. More recently, active ethanolysis products have been recovered from pine tissue cultures after administration of labeled shikimic acid (*25*), and two groups of workers have obtained further supporting evidence for the participation of the shikimic acid pathway in lignin biosynthesis, by feeding to plants glucose specifically labeled with carbon-14 (*26, 27*). From the lignin formed by spruce from this glucose they recovered vanillin labeled as would have been predicted if lignification had proceeded by way of shikimic acid. Russian workers have found that labeled pentoses, too, can act as lignin precursors (*28*).

On the basis of the work reviewed above and elsewhere (*29*) on the biosynthesis of lignin and other plant constituents, it seems clear that the shikimic acid pathway is involved in aromatic ring formation in higher plants, and that it is at least closely similar to that established in *Escherichia coli*. It is less certain that this is the only way aromatic lignin precursors are formed from carbohydrates. A route to certain aromatic compounds involving the condensation of three molecules of acetic acid is known to exist in plants (*29*), but there is evidence that its significance in lignification is slight (*25, 27, 30*). Other

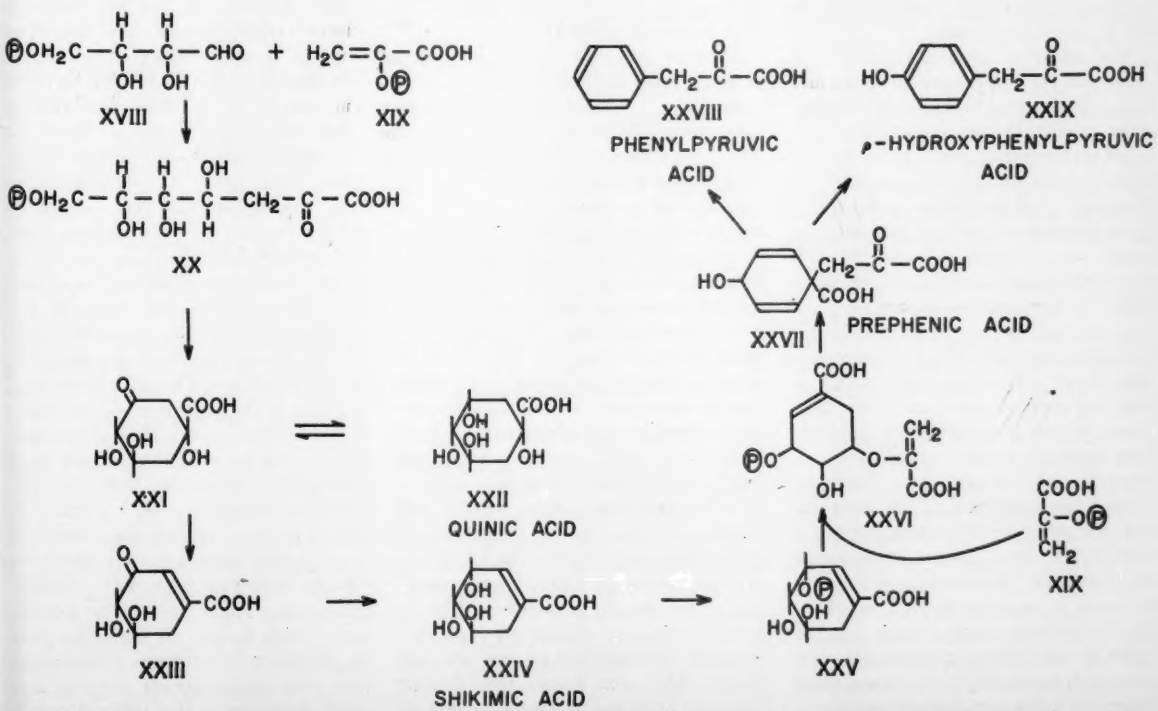


Fig. 4. The shikimic acid pathway of aromatization operating in *Escherichia coli* (P=PO_3H_2).

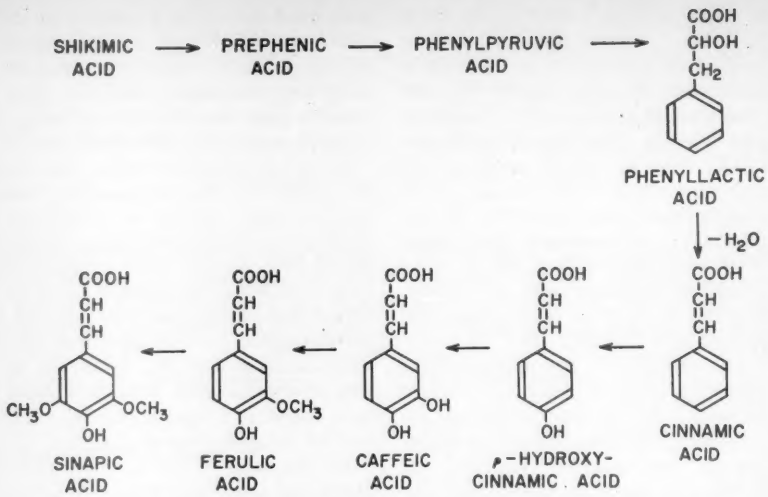


Fig. 5. A possible route for the formation of phenolic cinnamic acids in the plant.

routes to phenylpropanoid compounds have not been ruled out. Recently Weinstein, Porter, and Laurencot (*31*) showed that when quinic acid (Fig. 3, XXII) was fed to roses, the carbon-14 in phenylalanine reached a peak before that of shikimic acid. This may indicate that shikimic acid here is not on the direct route between quinic acid and phenylalanine, which can be formed from phenylpyruvic acid by transamination, or possibly that an alternative pathway is operating independently of the shikimic acid route.

The origin of the methyl carbons of lignin has been shown by Byerrum and his co-workers (*32*) to be the methyl group of methionine, and ultimately the 1-carbon metabolic pool. Thus, we can account with reasonable certainty for the origin of all the carbon atoms in the lignin monomers, and we can now examine the question of how the first phenylpropanoid compounds are converted to lignin monomers.

In working out biosynthetic pathways a fruitful approach can be a comparison of the efficiencies with which a large number of compounds are converted to the component in question. This approach is most useful when radioactive compounds are available. From a consideration of the most efficiently utilized compounds (there is often a difference of one or more orders of magnitude) it is often possible to arrive at a working hypothesis about the biosynthetic route, which can be tested by the feeding of additional compounds. It is necessary also, when using tracers, to carry out degradations to locate the position of the tracer in the molecule and eliminate the possibility of breakdown and resynthesis. The two approaches are both essential for the most rigorous demonstration of a precursor. The tracer technique cannot by itself establish a compound as an obligatory intermediate in a pathway, but the participation of naturally occurring compounds can often be demonstrated. When several such intermediates have been identified, studies on the plant enzyme systems can be undertaken to confirm the individual steps in a proposed pathway.

Various potential lignification intermediates have been compared by Brown and Neish (*3, 18, 23, 30, 33, 34*), who used tracer techniques, and by Stafford (*35*), who used unlabeled compounds. The former workers were able to eliminate several compounds as contributing significantly to lignification; these included acetate, C_6C_1 compounds in general, and C_6C_3 compounds bearing hydroxyl groups on the 3- and 2,3-carbons of the side chain, or in the *meta*-position only of the ring. On the other hand, a number of other C_6C_3 compounds were much more efficiently utilized: phenylalanine, phenylpyruvic acid, phenyllactic acid, cinnamic acid, and four hydroxylated cinnamic acids—*p*-hydroxycinnamic, caffeic, ferulic, and sinapic. On the basis of these findings it was proposed (*3*) that the formation of these compounds proceeded according to the sequence shown in Fig. 5. Support for the second part of this sequence was obtained by McCalla and Neish (*36*), who found that labeled cinnamic acids fed to *Salvia* underwent successive hydroxylations and methylations to form the later members of the sequence. Thus far it has not been possible to demonstrate these reactions in cell-free systems. But Koukol and Conn (*37*) have very recently found in legumes an enzyme which removes from phenylalanine the elements of ammonia to produce cinnamic acid directly. This enzyme, originally called phenylalanase, has now been named phenylalanine deaminase. Thus, it is no longer necessary to postulate the participation of phenyllactic acid in lignification, although its involvement still remains possible. This compound can be converted by way of phenylpyruvic acid to phenylalanine in the plant (*29, 38*); results of the tracer studies can be explained in this way.

In the course of tracer investigations on various grasses another pathway to lignin synthesis was discovered (*18, 33*), in which tyrosine can serve as a lignification intermediate. This reaction may proceed through *p*-hydroxyphenylpyruvic and *p*-hydroxyphenyllactic acids (see Fig. 5), both of which are readily convertible to lignin in wheat. But an enzyme analogous to phenylalanine deaminase, named tyrase has been reported recently by Neish (*39*). This enzyme, found in significant amounts thus far only in grasses, reaminates tyrosine to *p*-hydroxycinnamic acid. Examination of over 20 plant species has shown that tyrosine is utilized as efficiently as phenylalanine only in grasses, although several other species can use tyrosine to a considerably lesser extent (*40*). Similarly, *p*-hydroxyphenylpyruvic acid, which is a lignin precursor in wheat and sugar cane, is much less efficiently utilized by spruce, buckwheat and *Salvia* (*3, 41*). It seems highly probable that the ability of grasses to lignify by the tyrosine route depends on their tyrase content. Grasses also contain phenylalanine deaminase (*39*) and can synthesize lignin by way of phenylalanine. The route to lignin through phenylalanine would appear to be of earlier evolutionary origin, as it is found in the gymnosperms as well as in the higher angiosperms. Phenylalanine-C^{14} fed to spruce yields both lignin degradation products and coniferin which are radioactive (*42*). Apparently only in grasses, representing a very high stage of development, has the alternative tyrosine pathway been fully evolved. Interestingly, it is among the Compositae, which occupy an analogous place in development among dicotyledons, that some utilization of tyrosine as a lignin precursor is also detectable (*40*).

The pathways leading from carbo-

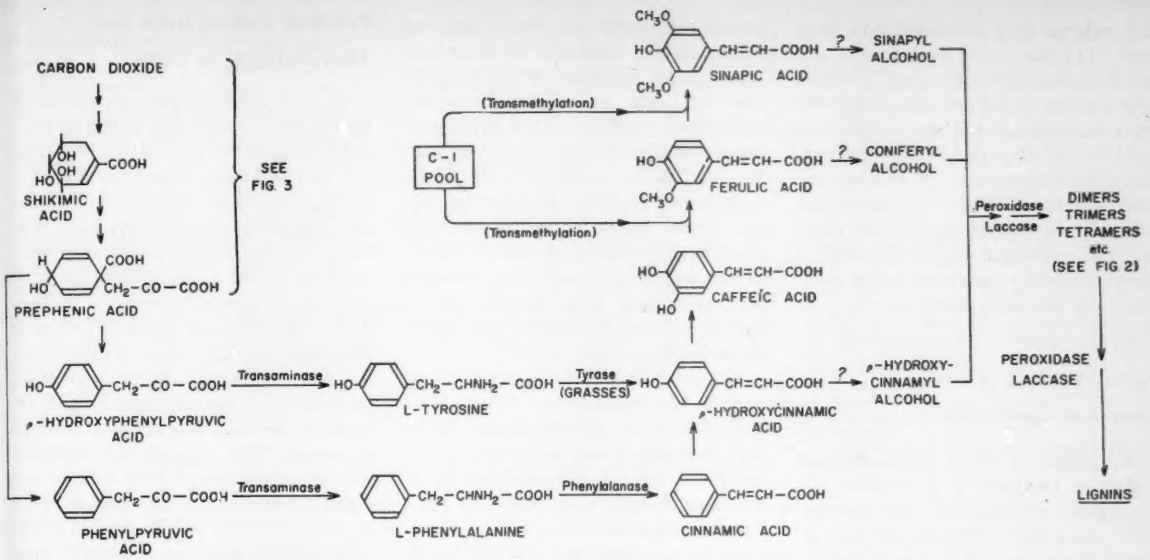


Fig. 6. Probable lignification pathways. Double arrows signify that more than one reaction is known to be involved. Not all these reactions occur in all species.

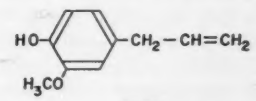
hydrates to lignin synthesis which are best supported by present evidence are shown in Fig. 6. This representation is still incomplete in several respects. Other routes to lignin remain possible, and this question is discussed in the next section. There is also no reference to the possible role of glucosides. The phenolic cinnamic acids are quite insoluble at the acid *p*H of typical plant saps, and in fact they must be administered to plants as salts. It would not be unreasonable to expect glucoside formation as an aid to translocation, as has been suggested already for coniferin, but reports that ferulic acid glucoside is a poor lignin precursor in spruce (*43, 44*) do not support this idea. Recently Higuchi and Brown (*45*) have found evidence that labeled ferulic acid fed to wheat can be chemically combined with glucose. The nature of possible "activated" forms of the intermediates has been largely a matter of conjecture. McCalla and Neish (*36*) found evidence for esters of substituted cinnamic acids in *Salvia*, and Levy and Zucker (*46*) showed that cinnamic acid in the form of a depside with quinic acid (Fig. 3, XXII) undergoes successive hydroxylation to chlorogenic acid, the corresponding depside of caffeic acid. Whether this process has any significance in lignification is not known. One serious gap in the reaction sequence of Fig. 6 is between the substituted cinnamic acids and the corresponding alcohols, which undergo the actual polymerization. In fact there is still uncertainty whether sinapic acid, as such, is an intermediate (*30*), and at least some of the extra hydroxylation found in the sinapyl-type lignin may be introduced after polymerization.

It should be pointed out that most of the steps shown in Fig. 6 are by no means peculiar to lignin biosynthesis. Flavonoid substances and coumarins, for example, are considered to be synthesized by the same route up to at least the cinnamic acid stage (*29, 47*). Clearly, too, the stages prior to phenylalanine and tyrosine must be viewed in the light of the relation of these amino acids to protein synthesis. Thus, these early compounds, such as *p*-hydroxyphenylpyruvic acid, can hardly be considered central intermediates in lignification. *p*-Hydroxycinnamic acid is a more likely candidate for that role (*3, 39*).

Other Possible Lignification Pathways

Although C_6C_3 compounds in general are not efficient lignin precursors, vanillin, which occurs in some plants, is utilized well enough to suggest that it may participate in a minor lignification pathway (*18, 30*). We might infer a condensation with some 2-carbon metabolite, but the nature of this hypothetical compound is not known. It has not been possible to confirm preliminary findings indicating that glycine (*48*) or acetaldehyde (*25*) is the 2-carbon compound in question.

Siegel, in a series of papers several years ago (*20, 49*), studied the polymerization of eugenol (XXX)



XXX

by several plant tissues in the presence of hydrogen peroxide. The amorphous product had solubility properties and gave color reactions characteristic of lignins. A number of considerations, such as the action of heat and enzyme inhibitors, the enhancing effect of hydrogen peroxide (up to 100-fold), and histochemical studies showing a correspondence between the sites of greatest polymerization and the most intense peroxidase activity, led Siegel to conclude that the polymerization is mediated by peroxidase. This agrees with the concept that peroxidase is one of the enzymes involved in natural lignification.

Although this is a very interesting model system, it is very doubtful that eugenol itself polymerizes. Eugenol undergoes ready spontaneous oxidation to coniferaldehyde (Fig. 2, IX) (*50*), and polymerization of this or a derivative probably leads to structures very similar to those reported by Freudenberg *et al.* Higuchi and Kawamura (*50*) found that freshly distilled eugenol was not converted to lignin-like polymers by peroxidases of bamboo shoot and horse radish, whereas the distillation residue

did undergo such polymerization. Stafford (*51*) has found that freshly distilled eugenol gives only small amounts of a polymer in the presence of timothy grass leaf sections but that ferulic acid yields large quantities of polymer similar to the natural lignin of that species. There seems no reason to believe that eugenol is a natural lignification intermediate; its formation in plants such as cloves doubtless represents a side reaction from the main pathway.

Factors Involved in the Control of Lignification

An intriguing aspect of lignification is that of the factors which exert the controlling influence on this process. Very young plants often appear to contain little lignin, and in wheat, for instance, lignification does not proceed at an appreciable rate until the plants are about ready to head out. What factors intervene to prevent or induce lignin synthesis?

The question whether photosynthesis is always necessary for lignification has not been fully answered. Kratzl (*52*), on the basis of three criteria—methoxyl content, solubility properties in acid, and oxidative degradation products—concluded that "a substance which doubtless can be classified as lignin" was formed in etiolated potato sprouts. This was in contrast to the results of early work by Klason, and also to the subsequent findings of Phillips (*53*), who showed that when ash shoots were shaded for periods of several weeks, the wood formed during this time gave only weak color reactions for lignin. The possibility that species differences may play a part here has not been excluded. The effect of light may be due to its influence on the supply of lignin precursors, such as intermediates of the photosynthetic cycle; an effect on other possible controlling factors is an equally plausible interpretation.

In any case, the availability of intermediates in the photosynthetic cycle cannot be the only factor controlling lignification, since much actively photosynthesizing tissue contains virtually no lignin. But it is quite possible that blocks at a later stage of the sequence imposed by the relative lack of a necessary enzyme or activator, or the presence of an inhibitor, can prevent lignification during certain periods of growth. Little is yet known about such possible control mechanisms. Kratzl (*54*) has reported the interesting observation that when syringin (glucoside of sinapyl alcohol) is fed to spruce, which normally does not make sinapyl-type lignin, the ethanolysis products of the lignin contain radioactive syringoylacetyl (Fig. 1, V; R=CH_3O), a sinapyl-type lignin degradation product. Perhaps the reason spruce cannot normally synthesize sinapyl-type lignin is that it is unable to convert ferulic acid to a sinapyl-type monomer, since ferulic acid is readily utilized by spruce for lignification (*43*).

Auxins appear to be involved in the control of lignification. Siegel (*49*) showed that the polymerization resulting from the action of *Elodea densa* tissues on eugenol was inhibited by 3-indoleacetic acid, which inhibited competitively oxidations catalyzed by peroxidase. He suggested that the high levels of this auxin in rapidly elongating organs would suppress peroxidase activity, and hence lignin deposition, whereas with the decline of auxin concentration that accompanies maturity, lignification would increase. Siegel and his associates (*55*) have concluded that 3-indoleacetic acid acts as an antioxidant to constrain peroxidase from a premature attack on metabolites essential to growth. Such a delaying action would prolong favorable conditions for growth, and when this is virtually complete, removal of the influence of the auxin could permit the onset of lignification in a given zone or throughout the plant. Other less-detailed reports (*56*) have suggested that in some tissues 3-indoleacetic acid can exert the opposite effect and stimulate lignification.

On the basis of measurements of glutathione and ascorbic acid in lignifying and nonlignifying parts of the bamboo shoot, Higuchi (*57*) believes that an oxidation-reduction system involving these compounds may be involved in controlling the amount of coniferyl alcohol available for the action of peroxidase in this species.

We could summarize by saying that the control of lignification is accomplished by the action of several factors, which may include the availability of intermediates from the photosynthetic cycle, the presence or absence of key enzymes or other factors involved in the formation of aromatic intermediates, and the presence or absence of oxidation inhibitors acting on the final polymerization steps. The relative importance of these factors undoubtedly varies from one species to another.

Cell-Wall Carbohydrates and Their Relation to Lignin

It is becoming generally accepted that lignin is chemically linked to polysaccharides in the cell wall (*2*, *58*). Thus far little is known about the biochemical aspects of this linkage, but one or two suggestive findings have been published. Siegel (*59*) has shown that when cellulose, in the form of filter paper, is added to a system of eugenol, peroxidase, and hydrogen peroxide, there is deposited on the paper a lignin-like polymer similar to that observed in the presence of tissue sections. In the absence of the cellulose no such material is formed. This suggests that lignification in natural tissues may also be intimately associated with the presence of preformed cell-wall carbohydrates. Freudenberg's group more recently have used other model systems containing mushroom laccase or manganese dioxide (*60*) to demonstrate that ethers can be formed between guaiacylglycerol coniferyl ether (Fig. 2, XI; R=CH_2OH) and sorbitol or sucrose. Siegel's findings are consistent with the possibility that ether formation may even be essential for lignification in the true sense. If so, it would be meaningful to conceive of lignification only in the broadest sense as those reactions leading to the formation of the lignin-carbohydrate entity which constitutes the cell wall.

Present Status, Future Prospects

Looking back over the work of the past decade, one can appreciate that very considerable strides have been made in our understanding of the biochemical pathways leading to lignin synthesis. As has been the case with other natural products, this has also furnished the structural organic chemist with important clues which would not have been available otherwise. The broad outlines of the lignification picture have been largely sketched in, but much detail remains to be added. Further developments can be expected in the isolation of more complex intermediates from the polymerization reactions and in the elucidation of linkages to polysaccharides of the cell wall. Additional tracer studies may lead to a bridging of the remaining gaps in our theories of the reactions by which lignin monomers are formed from carbohydrates. In this phase of lignification there is much scope for work in cell-

free systems, in which one can hope to demonstrate enzymes that would confirm more of the postulated reaction steps, or possibly bring to light still unsuspected reactions. A better understanding of the control mechanisms might open to us the possibility of regulating the formation of lignin, whose presence in many plants often leads at present to undesirable consequences. Another decade of research on lignification, if as successful as the last, may well provide us with a quite clear conception of this important process and provide extra dividends in the form of significant practical applications.

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Improving Scientific Communication

Reprints directly available from the publisher at a reasonable fee could supplement today's journals.

Jack Alan MacWatt

Alexis de Tocqueville (1805–59) wrote (*1*), "Americans of all ages, all conditions, and all dispositions constantly form associations." If anything is to be done in America, from constructing churches to sending "missionaries to the Antipodes . . . they form a society." This society framework aided the early scientists by bringing them together at regular meetings to exchange ideas and by giving them regular publications for reports on new discoveries. The growth of these two factors in the last century has changed the scientist and his methods of communicating.

Scientific Societies

The members of the American Chemical Society met for their 94th national meeting in September 1937. The *Abstracts* of the meeting listed authors and titles for 469 reports that were presented. The *Abstracts* of the 132nd meeting, held in September 1957, listed 1408 reports; the growth was 939 papers over the 20-year period.

A study of the list of periodicals abstracted by *Chemical Abstracts* shows that the 1926 edition reviewed a total of 1246 periodical titles. The American Chemical Society reports that over 9000 periodical titles were reviewed in 1960. This is an increase of more than 7700 titles in 34 years.

A U.S. Senate committee report (*2*) of 1960 states: "The science and technology collections of the Library of Congress have doubled approxi-

The author is librarian of the Lederle Laboratories Division, American Cyanamid Company, Pearl River, N.Y.

mately every twenty years for the past century and now number more than 1.5 million volumes of books and periodicals. Statistics from other sources indicate that research literature doubles every 8½ years. Figures relating to the growth of scientific journals in all disciplines reveal that the 1924 edition of the *World List of Scientific Periodicals* cited about 24,000 titles, the 1952 edition gave 50,000, and it is estimated that the total will reach 100,000 by 1979."

Effect of Increase

The old pattern of attending the meeting of a scientific society of one's choice and subscribing to its journal is no longer satisfactory. The scientist can no longer get complete coverage of the important reports in his field in this fashion. The U.S. Senate committee report (*2*) states, "More and more he [the scientist] is finding that discoveries and developments of great potential pertinence to his work may turn up in research areas far removed from his specialty." The field of organic chemistry has become so broad that in October of 1958 the editors of *Chemical Abstracts* subdivided section 10 ("Organic chemistry") into ten categories.

This refinement of scientific fields or areas of specialization brought with it an increase in the number of journals published. Therefore, the greater the number of journals available, the greater the number of references missed by scientists. The first solution developed for this problem might be termed the index-by-journal system. This was the reproduction of all the tables of contents of journals of interest to a specific science or profession.

In the early 1940's, the country's physicians were the first to be offered this type of assistance by the Friends of the Armed Forces Medical Library. This independent group provided funds to permit the library staff to arrange and reprint the tables of contents of the medical journals as they were received by the library. The tables of contents of journals were reset in a standard type and reduced in size to get a maximum number on a single page. The resulting publication, called *Current List of Medical Literature*, was first issued as a weekly in 1941. It grouped the journals in classes—anatomy, physiology, and so on—to permit a rapid review by the physician of a field or fields of interest.

Another venture into indexing-by-journal was the *Guide to Russian Scientific Periodical Literature*, started in January 1948 by the library at Brookhaven National Laboratories in Upton, New York. This provided English translations of the tables of contents of Russian periodicals.

Contents in Advance was one of the first index-by-journal ventures that used a direct reproduction of the tables of contents as printed by the journals. This was produced experimentally by Eugene Garfield. In 1956 he prepared a service for management: twice a month contents pages from over 100 management periodicals were reproduced. *Current Contents*, contents pages from pharmacomedical journals, was started in 1958, and this weekly publication now reprints the tables of contents of 550 foreign and domestic periodicals, covering more than 125,000 scientific articles annually.

Since 1949 many librarians for research organizations have introduced indexing-by-journal for the scientific staff. The scientists were asking to see an ever-increasing number of journals from routine circulation lists. The longer these lists became, the less able the librarians were to satisfy reader demands for current information. It usually took at least a month for each journal on such a list to reach three readers, and duplicate subscriptions provided only partial relief. With routine circulation lists, each reader had to wait until the journal reached his desk before he discovered new articles of importance to his work.

Reproduction of the tables of contents (*3*) was the best way to get information about new papers in the literature to all scientists at the same time. Methods available for the reproduction of print, such as the Xerox, were used to transfer the actual table of contents from a journal to Multilith plates. The Multilith plates and the Multilith machine then provided enough copies of each contents page. On request, an individual received copies of all the contents pages reproduced in this manner. This service gave each scientist the same information at the same time, and it put all circulation on a "first-come-first-served" basis.

Surveys were sometimes made after such a service had been available for a year or more. The following comments were typical.

1) "I've seen a piece of apparatus that I'm interested in mentioned in a magazine which I ordinarily wouldn't look at. This apparatus had modifications that have proved helpful to us."

2) "Consider 'table of contents' service practically equivalent to literature assistant. Keeps me up to the minute with work of competing groups. Well worth all the effort put into it."

New Problem from New Service

The index-by-journal service, whether supplied by a professional association, a commercial enterprise, or the organization for which the scientist worked, filled the need for access to newly published material. Articles and reports in many fields were now available to the scientist for checking on a routine schedule while in his own laboratory, office, or home. He soon discovered through this indexing-by-journal service, that the society journals he subscribed to were not carrying all the articles he needed for his work. His reaction to this knowledge was to drop his subscriptions. According to Richard H. Belknap (*4*), "the *J.A.C.S.* [*Journal of the American Chemical Society*] in 1933 had 17,500 subscribers but in 1958 had only 15,600." This is in direct contrast to the trend of society membership: there were 17,645 members in 1933 and 88,806 in 1959.

This index-by-journal service pointed up the fact that for an individual scientist to subscribe to one or two journals was not enough. Dropping a subscription was a financial relief but no solution.

Solutions Suggested

Scientists were cutting down on their subscriptions in favor of other methods of securing the articles they needed. The development of new machines for the purpose of making reproductions quickly, usually of printed office forms or letters, and the advertising and publicity given these commercial ventures, were noticed by scientists. They projected the uses claimed for these machines to their own literature problems. If reproductions could be made in an office why couldn't they be made in a library? There was an increase in the number of requests for copying facilities in libraries, and a portable machine that a scientist could take directly to

a library for making his own copies was developed.

A need of this magnitude usually erupts in the form of criticisms and suggestions. One such suggestion was made by Rinehart S. Potts in a "letter to the editor" (*5*). He stated: "We have all noticed how certain trade magazines include a postpaid return card, bound in with the material. By using this a reader may request copies of literature or sometimes even reprints of the articles. I have not noticed any application of this to the more professional journals or abstract journals and would like to suggest consideration of this idea: that such a card be bound in with an abstract journal, and arrangements be made to send the requestor a copy or photocopy of the full article referred to by a given abstract."

The suggestion of a cooperative solution to the problem was made by Eugene Garfield (*6*). He recommended that publishers in the United States organize an association to administer a royalty system and to grant permission for the reproduction of articles from all scientific journals.

Commercial Answers

A problem in one field often has a counterpart in another. The need for copies of single articles was noted by publishers of management periodicals early in 1959. The *Management Guide* announced in that year that reprints of articles would be made available in a special cost-per-reprint basis, or in groups according to subject area. *Sales Meetings* announced in its issue of 18 September 1959: "Perforated pages—to make it easy to tear out articles—proved to be a boon to readers. Now we've gone one step further. We've eliminated staples in the binding so that the magazine now opens up flat. New slotted binding offers improved 'tear-out', too. (Try it. See how easy it is to tear out the articles you want to file or pass on.)"

Current Contents established a special tear-sheet service to make articles from any table of contents printed in *Current Contents* available by direct request. This "original article tear sheet," or OATS, request was originally filled by tearing the actual article from the original publication. When a second request for the same article was received from a second reader, the *Current Contents* organization purchased a second copy of the journal from the publisher and sent tear sheets to the second reader.

The scientist now has access to bibliographic indexes that permit him to scan many publications. One such index was developed in 1960 and another has been promised for 1961. But when he needs a copy of a specific article from a specific journal he does not want to have long correspondence with the publisher in order to obtain it. The suggestions and the commercial trend point to the reprint as an answer.

New Problems

The increase that has occurred in the demand for reprints or copies of articles focused attention on the copyright question. Action on this question has been taken in Europe, where a German court case in 1955 (*7*) established that, under German copyright law, the reproduction of printed material for internal use by a corporation is illegal without permission of the copyright owner. An agreement reached between the Borsenverein des Deutschen Buchhandels and the Bundesverband der Deutschen Industrie provided that a higher subscription rate be paid if copies are to be made or that stamps be purchased and placed on separate copies as they are made. The Borsenverein sees to it that the authors and publishers get their share of the funds collected. No published analysis of the practicability of this system has appeared.

A reprint system as an alternative to the periodical system was the subject of a recent article by Ralph H. Phelps and John P. Herlin (*8*), who present a review of all the proposals made on this subject over the last decade. Phelps and Herlin report that objections to the idea of a reprint system have always been raised because such a system has been considered an attempt to change the present methods of scientific communication. The periodical system has too many basic advantages and too long a history to be tampered with at this time. No attempts have been made, according to these authors, to introduce a reprint service as a supplementary or additional service of the sort required by today's scientists.

The "working scientists cannot be bothered even to make a mark on a form to get the paper they are interested in," says J. D. Bernal in discussing the reasons for the nonacceptance of a reprint system. In 1948, at the Royal Society Information Conference in London, he had suggested the use of reprints as an alternative to scientific periodicals for the communication of scientific information. He reversed his position on this matter in 1959 at the International Conference on Scientific Information, in Washington, D.C., in part for the reason given in the statement quoted.

Another obstacle is the fact that two of the groups that should be most concerned with this problem, librarians and publishers, have made no attempt to come up with a solution. The two groups got together at a rare round-table discussion of general problems at the 1954 Cincinnati convention of the Special Libraries Association, but no representatives of the scientific press were on hand.

Conclusion

This is a new era, and the scientist of today is not working under the same conditions as the scientist of de Tocqueville's society. This is clearly stated in the recent *Outline of Long-Term Policy* of the Fédération Internationale de Documentation (*9*): "The problem of primary publication in science is becoming continually more aggravated as specialization proceeds. Many scientists, members of the appropriate learned society in their own country, receive its journal but are in fact interested in (and perhaps capable of understanding) only a small proportion of the papers it contains, while they do not receive directly contributions of immediate importance to them in a whole range of other journals published in other parts of the world."

The scientist has moved away from concern with a specific field of scientific interest in the direction of subject interest. A different type of access to scientific information is needed. The index-by-journal system was the tool that increased the scientist's ability to scan many journals. He was weaned away from the tradition of subscribing to one or two society journals. Through use of this scanning tool and of the newer ones introduced or announced in 1960, *Index Chemicus* and *Chemical Titles*, this trend of scanning by subject will be continued.

What are the chances of getting a reprint if you are interested? The chances are good if you are a manager, but if you are a scientist you must be patient. *Harvard Business Review* makes available reprints of any article in an issue for $1, but the entire issue costs only $2. *Chemical and Engineering News*, in its issue of 23 May 1960, announced the availability of reprints at a cost of 40 cents a copy; the complete issue costs 50 cents. *Dunn's Review* offers reprints for 20 or 30 cents a copy; the full issue costs 75 cents. These journals are not scientific, but their example points to a possible trend. Publishers of scientific journals may be able to utilize some of the new printing methods to bring reprint costs more in line with economic reality.

It should be possible to set up, in the near future, a procedure whereby one can either subscribe to scientific journals on a yearly basis or purchase single articles at a unit price. Such a system would give scientists greater opportunity to select reading material on the basis of subject and would provide greater return for publishers. It would also make the new scanning tools more valuable by increasing the availability of items discovered in them. A meeting of publishers, librarians, and scientists should be called to consider this next step, so necessary for improved scientific communication.

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Science and the News

The Test Ban Hearings: Congress Presses for Kennedy's Decision

The Joint Committee on Atomic Energy held three days of hearings on the problem of detecting underground nuclear tests, which added nothing to hopes of reaching a solution of the problem. As happened in a similar set of hearings last year (*Science* 29 Apr. 1960), the testimony was dominated by evidence that even if the control system embodied in the draft treaty presented by the U.S. and the British were put into effect, it would not guarantee that there would be more than a modest possibility that any given violation would be detected and exposed. There seems to be no serious dispute on this point among the scientists who have worked on the problem. Neither of the two scientists who produced the greatest impact at last year's hearing appeared this time. At the earlier hearing Hans Bethe, of Cornell, argued vigorously in favor of going ahead with a treaty; Edward Teller, of the Livermore weapons laboratory, argued equally vigorously against the treaty. But the two men were in general agreement on the technical points involved, with Bethe, in effect, agreeing with Teller that the proposed control system could not, by itself, assure that a violation would be detected. The disagreement between the two men stemmed from broader considerations of national policy affecting the wisdom of striving for an agreement rather than from a dispute over the technical adequacy of the control system.

These broader considerations included such things as the value to the Russians (and hence the temptation) to attempt clandestine testing, and the importance of test-ban agreement as a step towards broader disarmament agreements.

This year's hearings drew less public attention, partly because both Teller and Bethe declined invitations to appear again, on the grounds that they were not closely familiar with the research that has been conducted since the earlier hearings. The essential point of the testimony of those who did appear was that as yet no major technical breakthrough had been made that would greatly simplify the problem of detecting tests.

On the political side, Arthur Dean, the chief American negotiator at Geneva, appeared at the closing session to outline what presumably is the Administration position. He reviewed the dismal course of the negotiations since they resumed last March. He said we were still prepared to sign the draft treaty we had offered, and that despite the technical testimony on the adequacy of the control mechanism, both British and American scientific advisers agreed that it would provide "reasonably adequate" controls, presumably when supplemented by intelligence from outside the technical system which would help decide which unidentified events should be investigated. Dean described how, after the Russian scientists had agreed on the need for a research program, including nuclear explosions, the Russian political leaders, after the summit collapse last spring, had overruled their scientific advisers and decided that the research program was not necessary after all; how the Russians had, since March, not only failed to offer any counterconcessions to the concessions included in the Western draft treaty on the number of inspections and other matters, but had backed down on agreements already reached, most notably through their new insistence on a veto over the administration of the control mechanism.

Dean, nevertheless, argued that the talks should continue, and that Project Vela, the Defense Department's detection research program, should be pushed. Dean stressed, as he has in private briefings with reporters in recent weeks, that there is always a pos-

sibility that the Russians will have another change of mood, and that therefore we ought to be very patient and continue talking as long as the Russians are willing to talk. He cited the case of the Austrian peace treaty of 1955, where, after extremely protracted and discouraging negotiations, the Russians quite suddenly changed their mood and a treaty acceptable to both sides was quickly worked out.

But on this point committee members from both parties raised the point that whereas on the Austrian treaty we had nothing to lose by talking indefinitely, on this matter there are substantial risks involved in continuing the talks indefinitely if that means we are going to continue the present unpoliced moratorium on testing indefinitely. "My heart goes out to the President," said Senator Pastore of Rhode Island. "This is a terrible decision he has to make. But he has the responsibility, and he is going to have to make a decision."

Committee Attitude

The Joint Committee has, for a long time, taken a dim view of the possibility of agreeing on a satisfactory treaty, and last year's hearings were intended to publicize the committee's concern over the immense technical problems of designing a satisfactory control mechanism. But the Administration has apparently convinced the committee that its draft treaty was a reasonable balancing of the risks involved in continuing the ban, and until recently committee members from both parties had avoided making public statements over their misgivings. At the hearings, chairman Chet Holifield, of California, revealed publicly for the first time that the committee had agreed to go along with the Administration and recommend to Congress changes in the Atomic Energy Act which would allow the Administration to let the Russians inspect the devices to be used in the proposed detection tests, in order to assure themselves that we were not conducting clandestine weapon tests ourselves. This involved no real concession, since the Russians could learn nothing they did not already know from the devices, but Holifield pointed out that this was nevertheless a politically awkward thing for the committee to do, since there were bound to be charges that we were giving away atomic secrets to Russia, while we would not show the devices to our own allies. Holifield's point, of course, was that despite the committee's misgivings, they were not only prepared to support the Administration but even to stick their necks out to cooperate on a delicate political issue. Now, despite the committee's reluctant cooperation, things have gone from bad to worse, and the committee clearly expected the President to make his tough decision and either to resume testing or to supply the committee with a convincing new argument over why we should not.

Within the Administration, though, there was no rush to resume testing. For one thing, world opinion appears to have become sympathetic to the American view on the issue for the first time, and a good part of this change in mood has stemmed from the elaborate display of patience the West has shown since the talks reopened in March. The result was that the American White Paper on the dispute issued in June, culminating in a reminder to the Russians that the U.S. could not allow the current unpoliced moratorium to continue indefinitely, impressed much of the world as an unavoidable response to Russian recalcitrance rather than an attempt to find an excuse to resume testing.

Under the treaty the West has proposed, at least 2 years would pass after the ratification of the treaty before the control system would be ready for operation. The Administration, and the Joint Committee for that matter, presumably must have been convinced, then, that the risks in continuing an uninspected ban for two more years would not necessarily be unacceptable. One thing that would make these risks acceptable, of course, would be a signed treaty, but even under present circumstances there are good, though perhaps not compelling, reasons for taking some risk to avoid a prompt resumption of testing: for example, to avoid any impression of eagerness to take such a serious step, and, at the present moment, to avoid confusing the world about our motives in instituting a defense build-up to meet the Berlin crisis by taking almost simultaneously another tension-provoking step that has no connection with the immediate crisis. Thus, the general mood in Washington is one of great pessimism over the course of the Geneva negotiations, but despite congressional restiveness, this mood is not accompanied by an expectation that an announcement to promptly resume testing is likely.———H.M.

News Notes

Solid and Liquid Propellants

Astronaut Virgil Grissom's recent suborbital ride in space took only 15 minutes, but 2 days of additional preparation were required when his flight was postponed because of poor weather. Weather alone might have held up the flight only a few hours. It was the use of liquid fuel to propel the Redstone launch vehicle that forced the extended delay.

The Redstone uses liquid oxygen, which boils at −185° C. It is difficult to maintain this low temperature in the Redstone rocket, in which insulation is limited because of weight. A slight rise in temperature of only a few degrees above the boiling point is considered hazardous and also means loss of fuel from evaporation. Such a temperature rise may be reached 7 to 8 hours after the rocket is fueled.

The Redstone rocket was fueled 2 to 3 hours before scheduled take-off, allowing a maximum delay of 5 hours. When the delay went beyond 5 hours, it was necessary to remove the liquid oxygen and to begin a tedious 2-day procedure of washing, drying, and checking the rocket engine for contamination before refueling. Even a speck of dirt may clog a valve.

Such procedures are costly in time, money, manpower, and material and have prompted criticism of the continued emphasis on liquid fuels in the national space effort. But such criticism fails to take into account the important advantages afforded by liquid-fuel engines that, at the present stage of the art, far outweigh the penalties imposed. Liquid fuels are more powerful and permit better guidance and control.

The power of a booster is measured by its specific impulse—the number of pounds of thrust released by each pound of burning fuel per second. Liquid fuels presently available have a specific impulse as high as 430; most solid fuels operate with a specific impulse of 235 to 240. A solid fuel with a potential of 290 is still under development.

Guidance and control can be maintained in a liquid-fuel system by the complex of pumps and valves that makes it possible to limit the flow of fuel into the combustion chamber and, if desired, to cut it off entirely. Such control is important in getting a vehicle

through the atmosphere, where winds may affect a planned route and may require a change in rate of acceleration. In solid-fuel boosters the rate of acceleration is fixed. Some measure of control may be provided by segmenting the solid fuel with inert material which will cut off energy at predetermined intervals, and by a device that will reignite the rocket on command from the ground.

The major advantages of solid-fuel boosters are ease in handling, low cost, and reliability, because of their comparatively simple design and construction. They are self-contained and can be held indefinitely on a launching pad without hazard. A launch vehicle using solid-fuel boosters can be reloaded and rechecked in a matter of minutes. There is no evaporation of costly fuel; and, since there is no need for valves, pumps, and other moving parts, solid-fuel engines can be produced at about one-third the cost of their liquid-fuel counterparts.

Most nations now developing launch vehicles for space research (among them Japan, Great Britain, Australia, and Israel) have turned to solid fuel because of these advantages, particularly that of low cost. There is reason to believe that the U.S.S.R. has not neglected this technology.

Canada has developed a family of three solid-fuel research rockets capable of carrying scientific payloads of up to 250 pounds to altitudes of 600 miles. She is currently trying to interest the National Aeronautics and Space Administration and the U.S. Department of Defense in the all-solid-fuel two-stage systems, as part of a bilateral defense and research-sharing program. The Department of Defense already has an extensive family of highly reliable solid-fuel boosters, including the Minuteman, the Cajun, and the Polaris. NASA has developed the Scout, a four-stage solid-fuel engine capable of putting a 150- to 250-pound payload into orbit at 300 miles altitude or a 50-pound payload into orbit at up to 8400 miles altitude.

In the United States, several companies, some independently and some with government sponsorship, are working to develop large, solid-propellant rocket engines. This fall United Technology Corporation plans to test-fire a solid-fuel engine of half a million pounds thrust. Last July the same company successfully fired a two-stage solid-fuel booster with a thrust of 250,000 pounds. It was developed independently at a cost of $5.5 million. Four firms now are seeking government contracts to produce solid propellants for the third stage of the Nova space rocket, which is being designed for NASA and the Air Force for the primary purpose of landing a man on the moon. Although still on the drawing board, plans are to use a cluster of eight liquid-fuel F-1 engines, of 1.5 million pounds thrust each, for the first stage. Hopes are that the Nova will be operational by 1970.

Work is now under way on the Saturn C-1 vehicle, a three-stage liquid-propellant rocket of 1.5 million pounds thrust. It is scheduled to be operational in 1964 and will be able to put 7-ton payloads in orbit. Proponents of solid-fuel engines claim that a concentrated research and development program, with government support, would yield by 1964 a booster with a thrust in excess of 2 million pounds. The present Administration has allotted $50 million for research in large solid-fuel engines to the Air Force, which now has the main responsibility for developing large boosters.

If large solid-fuel boosters with a specific impulse comparable to that now available with liquid fuel can be developed, the ideal launch vehicle for heavy payloads and deep excursions into space could be built. This vehicle would combine the reliability and economy of solid-fuel boosters, in the first stage, with the ease of control attainable with liquid-fuel engines, in the upper stages.

Atomic Attack: Alert, and Shelter

In his speech on Berlin, President Kennedy said those not hit by a nearby nuclear blast "can still be saved—if they can be warned to take shelter and if that shelter is available." Within 24 hours thereafter, the following government action was taken to provide the necessary warning and shelter. The Administration asked Congress for $10 million to put into operation a National Emergency Alarm Repeater (NEAR) buzzer system which will furnish each home, office, and factory with a direct alarm for any impending attack or disaster. The Department of Defense outlined plans to set up completely stocked fallout shelters in basements and hallways of existing large office, industrial, and apartment buildings at a cost of $169 million. The Federal Housing Authority ruled that family fallout shelters may be built under FHA home improvement loans up to $10,000 at an interest rate not to exceed 6 percent, to be financed over a 20-year period.

According to Civil Defense officials, NEAR would make it possible to alert the entire nation within one minute after a signal from the Air Defense Command. The system is housed in a small black box that can be plugged into any 110-volt circuit. Through the local power company, it will sound a loud buzzer for 50 seconds, with a 10-second pause between signals, by superimposing a 240-cycle signal on the regular 60-cycle current until the danger has passed. The buzzer is intended to alert listeners to turn on the radio to Conelrad frequency—640 or 1240 kilocycles—for civil defense information. The $10 million requested by the Administration is intended for special equipment for the utility companies to produce and send out the 240-cycle signal. The black box device, developed by General Motors after 5 years of research, will sell at a retail price of $5 to $10.

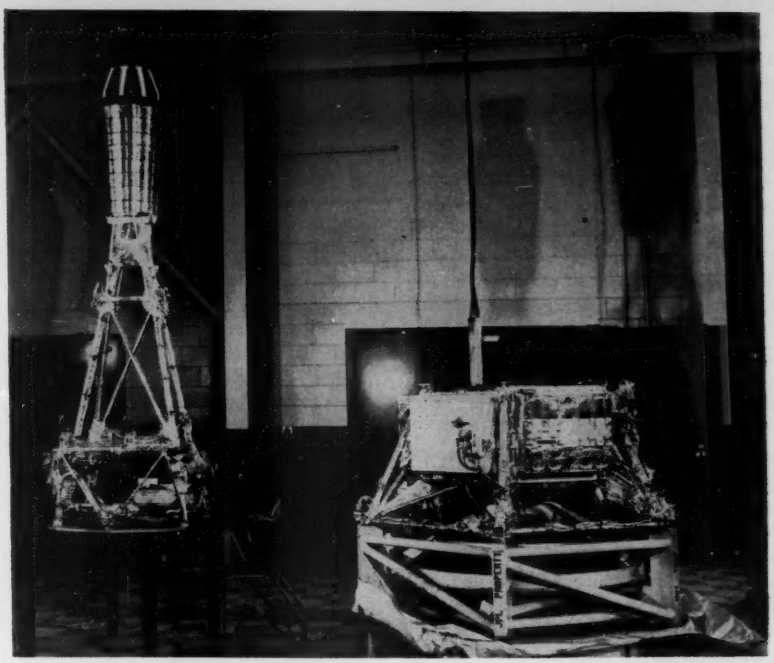
Government plans for fallout shelters do not include any for single-family dwellings. The first shelters probably will be set up in government buildings and will be stocked with radiation-measuring equipment, first-aid kits, sanitary supplies, and tools for clearing debris, in addition to a 5-day supply of food and a 2-week water supply.

Only a relatively few private-family fallout shelters have been built in the United States, but interest has greatly increased since the Berlin crisis, a Civilian Defense official said. Prior to the new ruling, loans for shelters were limited to $3500, repayable over 5 years, at interest rates over 9 percent. Under the old program, only 235 loans for fallout shelters have been approved by the FHA, all in the Great Plains states, where the shelters have been useful for protection against the recurrent threat of tornadoes. To qualify for FHA loans, the shelters must satisfy building specifications set up by the Office of Civilian Defense Mobilization as well as pass FHA inspection. Fallout shelters qualify for loans under home improvement because, as the official FHA announcement stated, such facilities improve the basic livability of a home.

Step to the Moon

The successful launch of the Ranger space craft this week, which may put it into orbit around the sun, is a major step forward in the National Aeronautics and Space Administration program for exploring the moon. The trajectory planned for the test flight should place Ranger in an elliptical earth orbit as far as 500,000 miles and as close as 37,500 miles before it returns, in about 50 to 100 days, to burn up in the earth's atmosphere; but it is possible that the launching rockets may speed Ranger to an earth-escape velocity that will place it in orbit around the sun.

The launch was designed to test the vehicle NASA hopes may be the forerunner of space craft capable of landing instruments on the moon, and the mechanics of a parking orbit, in which a second-stage rocket is used as a mobile launching platform in space. The parking-orbit technique was devised to correct the navigation problems imposed, in shots aimed at the moon, by the location of the Atlantic Missile Range. The Ranger probe also will test a basic hexagon-shaped space "bus" (see cut), which will carry as many as eight scientific projects on Ranger missions. The bus and its equipment are standard and can be adapted to many studies. Electronic equipment in the bus carried by Ranger I will telemeter back to earth data on the nature and activity of cosmic rays, magnetic fields, radiation and dust particles in space, and other phenomena believed to result from variations in solar activity.



Basic hexagon space bus, at right, carried by the first Ranger satellite. Both hexagon and Ranger, at left, were developed by the Jet Propulsion Laboratory operated by the California Institute of Technology for NASA. [National Aeronautics and Space Administration]

The domestic art of hand quilting is being used in the construction of the $29-million **Zero Gradient Synchrotron** (ZGS), a 12.5 billion electron volt "atom smasher" at Argonne National Laboratory, which will be able to produce all known subatomic particles believed to form the basis of matter. An atomic-age seamstress, using an ordinary needle and cotton thread, will spend about six months stitching and quilting 25 to 70 layers of chemically treated Fiberglas, cut in patterns, to line the 16 transition chambers. Two hundred yards are required for each of the chambers, which serve as links to the magnet-encompassed vacuum, the heart of the synchrotron, where the particles will be accelerated and studied for reactions. The Fiberglas quilting reinforces the vacuum.

When completed, the ZGS will produce greater numbers of accelerated subatomic particles than any other multibillion-volt atom smasher now in operation or under construction.

Brookhaven's **Alternating Gradient Synchrotron** accelerated a beam of protons to an energy of 33 billion electron volts in its first full series of basic physics experiments last week, in which it ran at full power for three consecutive days. This is the highest energy achieved by any accelerator.

The AGS will have to shut down for several weeks while thousands of tons of shielding are moved, equipment is realigned, and special beam separators are installed for the next research project. Each series of experiments may require different configurations, so the accelerator facility has been built to permit changes. An overhead crane and tracks in the floor facilitate the heavy moving job.

Nearly as powerful as the AGS is the 25-Bev synchrotron operated by CERN, the European nuclear research agency near Geneva. The Russians have a 10-Bev machine at Dubna, near Moscow, and have announced plans for constructing a 50-Bev accelerator near Leningrad. Other large atom smashers are the 6-Bev Bevatron at the University of California, Berkeley, the 4-Bev Cosmotron in Saclay, France, and the 3-Bev Cosmotron at Brookhaven in Upton, Long Island, New York.

The **National Science Foundation budget** will be up 60 percent in the current fiscal year. Eisenhower had recommended a $34-million increase over last year's $175 million. Kennedy's budget revision recommended another $65 million. Representative Thomas's (D-Tex.) House appropriations subcommittee recommended its customary 10-percent cut; the Senate appropriations committee made its customary recommendation restoring almost everything that Thomas had cut. The Senate passed its version of the bill this week. A conference will compromise the difference, leaving the NSF with about 5 percent less than the Administration has recommended but, at around $263 million, still $87 million above last year's budget.

The U.S. has given $350,000 to Greece for its **atoms-for-peace** program to help pay for the recently completed 1-thermal-megawatt pool-type research reactor at the Democritis nuclear research center near Athens.

The reactor achieved criticality last month. Ten other nations have received such U.S. aid. They are Austria, Brazil, the Republic of China, Denmark, West Germany, Italy, Japan, Spain, Venezuela, and Norway.

Last month the **United Arab Republic** also **produced a nuclear reaction** in its reactor of 2000-kilowatt power, built near Cairo with the help of the U.S.S.R. Selah Hedayet, director of the UAR's atomic energy commission, in announcing the reactor's operation, said it will be used for peaceful purposes.

AT&T and NASA have signed a contract permitting the telephone company to sponsor the launching of two experimental **communications satellites**. The space agency will launch the satellites for AT&T. AT&T will pay for both the satellite and the launching, and will allow NASA royalty-free use of any patents developed out of the experiment. NASA itself hopes to launch about ten experimental "relay" satellites, similar to AT&T's. RCA, AT&T, and five other firms had bid for the NASA contract. NASA chose the RCA approach, after which AT&T, apparently convinced its version was superior, asked to be allowed to put up its version at its own expense.

Earlier last week the Federal Communications Commission, which regulates privately owned communications systems, asked the consortium of private companies that has been invited to work on a satellite proposal to come up with a detailed proposal, including such things as the amounts of money they are prepared to invest, "as soon as possible, but in any event no later than 13 October."

An Air Force plan to shoot a cloud of **350 million inch-long metal needles** into a 2000-mile orbit to serve as a passive communication system has alarmed astronomers, who fear the needle belt may obscure optical and audio observations in space. The needles, thinner than a human hair, would serve as miniature antennas to reflect radio signals from earth. Optical astronomers fear the needle cloud might obscure stellar observation by astronomical satellites. Radio astronomers are concerned that it might interfere in radio signals from stars. As a result of protests, the matter has been referred to the National Space Council for study and a policy statement.

Announcements

The nation's first statutory **interstate nuclear agreement** became effective in June when Florida became the seventh state to ratify the agreement, the minimum number required to bring the compact into effect and create the Southern Interstate Nuclear Board. The present members are Florida, Arkansas, Kentucky, Louisiana, Tennessee, Texas, and South Carolina. The compact offers the means whereby the southern states may "concert their energies and talents, both public and private, in developing the atom for optimum peaceful applications in industry, agriculture, medicine, and research." The Regional Advisory Council on Nuclear Energy (RACNE), established in 1956 as the "first nonfederal, publicly supported, interstate nuclear-energy organization in the nation," will continue to serve the nine remaining southern states until they ratify the compact and become members. RACNE will then go out of existence.

Starting in September, NBC-TV's 6:30 A.M. "Continental Classroom" will present a two-semester graduate course on the structure and function of **American government**, taught by Peter H. Odegard of the University of California. At 6 A.M. each week day NBC will repeat the 1960–61 course in **contemporary mathematics**, taught by Frederick Mosteller of Harvard University and John L. Kelley of the University of California.

A formal educational program in **scientific hydrology** will begin next fall at the University of Arizona. The program, reported to be the first of its scope in the United States, will lead to the B.A., M.A., and Ph.D. degrees in this field. (Department of Geology, University of Arizona, Tucson)

A Soviet study on various phases of research in **processing scientific information** reveals that some Russian scientists spend "nearly half their working hours trying to keep abreast of the latest developments in their field." The report, published by the Soviet Academy of Sciences' Institute of Scientific Information, also cites a number of American studies on the subject. The Russian analysis of the reading habits of Soviet chemists coincides in certain respects with the conclusions reached by a 1960 study, sponsored by the National Science Foundation, of the same problem as it affects American chemists and physicists [*Science* **133**, 2019 (23 June 1961)]. (Office of Technical Services, U.S. Department of Commerce, Washington 25, D.C. Order No. 61-31465, $1.50)

Information of scientific or political interest on the **Antarctic** is being sought by Science Communication, Inc., in connection with a survey sponsored by the National Science Foundation's Office of Antarctic Programs. The information may be in the form of published reports, diaries, unpublished scientific data, expedition log books and other documents, telemeter tapes, or biological and geological specimens or artifacts. (Antarctic Information Project, Science Communication, Inc., 1079 Wisconsin Ave., NW, Washington 7, D.C.)

The Atomic Energy Commission has published a summary of **atmospheric radioactivity and fallout research** in progress at 36 institutions in the United States. (Office of Technical Services, U.S. Department of Commerce, Washington 25, D.C. $0.75)

Anecdotal material, letters, and other manuscripts which would be helpful in preparing a **biography of Albert Deutsch**, a journalist specializing in psychiatric research who died in June, are being solicited by the newly formed Albert Deutsch Memorial Foundation. The foundation plans, also, to publish a memorial volume of Deutsch's writings and to establish an annual journalists' award. (Deutsch Memorial Foundation, Room 1130, Dupont Circle Bldg., Washington 6)

Results of a recent survey on **current trends in scientific research** have been compiled by the United Nations Educational, Scientific and Cultural Organization. (UNESCO Publications Center, 801 3rd Ave., New York 22, $6.75)

Publication of a new paperback **Science Editions series**, for students and general readers, will be jointly sponsored by John Wiley and Sons and Basic Books. The first ten volumes, priced from $1.45 to $2.45, are scheduled to appear in September. (Belfour McMillan, Science Editions, 440 Park Ave. South, New York 16)

Recent achievements and future goals in **Soviet engineering** and engineering education and manpower utilization are presented in a report published by the Engineers Joint Council. *The Training, Placement and Utilization of Engineers and Technicians in the Soviet Union* is based on the report of an Engineers Joint Council delegation to Russia in July 1960, under an exchange agreement between the U.S. and the U.S.S.R. (Engineers Joint Council, 29 W. 39th St., New York 18)

Courses

A 1-week course in **cancer chemotherapy**, sponsored by the Sloan-Kettering Institute for Cancer Research, will be held at Cornell University 23–28 October. The course will review the clinical problems and recent advances in the chemotherapeutic management of the leukemias, lymphomas, and the major forms of carcinoma. Applications should include a brief summary of clinical training and current appointments. (D. A. Karnofsky, Sloan-Kettering Institute, 410 E. 68 St., New York 21)

A 2-week institute in **experimental stress analysis** will be given by Wayne State University, 11–22 September. The courses will cover photoelasticity and the use of strain gages. (Joseph Der Hovanesian, Department of Engineering Mechanics, Wayne State University, 655 Merrick, Detroit 2, Mich.)

Three seminars in the **space sciences** will be held at the University of California, Berkeley, 4–15 September. The general areas to be covered include interplanetary particles and fields; space biophysics; and planetary environments and extraterrestrial life. Registration may be made by individuals or companies. Deadline: *25 August*. (Engineering and Sciences Extension, University of California, 2451 Bancroft Way, Berkeley 4)

Scientists in the News

Col. **Adam J. Rapalski**, epidemiologist and commanding officer of the Army Environmental Hygiene Agency, Army Chemical Center, Md., has been appointed chief of the Army Surgeon General's Preventive Medicine Division. He succeeds **Arthur P. Long**, who retired to become professor of environmental medicine at the University of California Medical Center, San Francisco.

Recently appointed Fulbright lecturers for 1961–62:

James P. Danehy, associate professor of chemistry at the University of Notre Dame, will lecture at the National University of Ireland, University College, Cork.

A. K. Snelgrove, head of the department of geology and geological engineering at the Michigan College of Mining and Technology, will lecture on economic geology at the University of Sind, Nyderabad, West Pakistan.

Maurice Goldhaber, chairman of the physics department at Brookhaven National Laboratory, has been named director of the Laboratory. He succeeds **Leland J. Haworth**, who was appointed to the U.S. Atomic Energy Commission in April.

David Glick, professor of physiological chemistry at the University of Minnesota Medical School and director of the university's Histochemistry Laboratory, has been appointed professor and head of the department of pathology at Stanford Medical School.

H. Borden Marshall, director of the Ontario Research Foundation's department of chemistry, Toronto, Canada, has been selected to receive the Montreal medal of the Chemical Institute of Canada. The award will be presented during the 44th Canadian Chemical Conference and Exhibition in Montreal, 3–5 August.

Laurence H. Snyder has resigned as president of the University of Hawaii. Snyder, a geneticist, was president of the AAAS in 1957.

Recent additions to the Washington, D.C., research staff of the Massachusetts Institute of Technology's Operations Evaluation Group:

Robert L. Hubbard, lecturer in physics at the University of North Carolina.

Edgar R. Terry, senior mathematician at Vitro Laboratories, Silver Spring, Md.

Thomas E. Moon, an engineer who became blind in 1945, will receive the 1961 Holley medal of the American Society of Mechanical Engineers for his invention of a trephine for corneal transplants and of other surgical instruments.

Leonard Karel, former chief of the extramural programs branch of the National Institute of Allergy and Infectious Diseases, has been appointed special assistant to the associate director for research of the National Science Foundation.

Henry van Zile Hyde, chief of the U.S. Public Health Service's division of international health, has been named director of the new division of international medical education of the Association of American Medical Colleges.

Recent Deaths

John B. Cross, 61; chairman of the department of obstetrics and gynecology at Emory University since 1945; 23 July.

Elmer A. K. Culler, 71; professor emeritus of psychology at the University of Rochester; 30 June.

Louis H. Douglass, 72; obstetrician and surgeon, and former professor of obstetrics at the University of Maryland School of Medicine; 23 July.

Carlyle S. Fliedner, 72; inventor in the field of aircraft propulsion systems and for 32 years aeronautical engineer with the Navy Department's Bureau of Naval Weapons; since his retirement in 1958 had served with the bureau as a consultant; 11 July.

Lawrence W. Jenkins, 88; anthropologist and director emeritus of the Peabody Museum; 20 Apr.

Paul W. Merrill, 73; astronomer at California Institute of Technology's Mount Wilson and Palomar Observatories for more than 40 years; 19 July.

Atherton Seidell, 82; research chemist associated with the Pasteur Institute, Paris, and the National Institutes of Health, Washington, D.C.; 25 July.

Lester W. Sharp, 74; emeritus professor of botany at New York State College of Agriculture; 17 July.

E. Edwin Weibel, 64; member of the engineering faculty at the University of Colorado since 1947; 16 June.

Erratum: In the report "Correlation of nuclear volume and DNA content with higher plant tolerance to chronic radiation," by A. H. Sparrow and J. P. Miksche [134, 282 (28 July 1961)], the figure 3000 on the vertical axis of the graph in Fig. 1 should read 10,000.

Book Reviews

Is Political Science a Science?

Political Science. A philosophical analysis. Vernon Van Dyke. Stanford University Press, Stanford, Calif., 1960. xv + 235 pp. $5.

There has been much debate whether the social sciences in general and political science in particular are real sciences. Some natural scientists think they are not because they are intended to assist in making decisions which involve value judgments while the function of science is to produce generalizations which give information as to what will happen under stated conditions or what measurable relations can be relied upon among defined variables. Social scientists, however, reply that while they cannot ignore values they can discover persistent relations, statistical trends, and effective methods of exerting influence, and that the information and classification of this knowledge constitutes science. While they recognize that they frequently have to deal with qualitative distinctions, they increasingly seek to reduce their distinctions to quantitative terms. This is especially true of the economists and sociologists, but in recent times the political scientists have also utilized statistics. They can conform in a measure to Lord Kelvin's suggestion that if it cannot be measured it is not a science.

Vernon Van Dyke, who writes from long experience in conducting a graduate seminar on the philosophy of political enquiry, does not argue the point but assumes the broad view that science is the acquisition, verification, and systematic classification of useful knowledge. He recognizes the importance of the knowledge being as general as possible and the difficulty of utilizing this criterion in the social sciences where there is frequent incompatibility between the requirement of verifiability and the requirement of generality (page 196).

The utilitarian point of view which he suggests conforms to the title of "The American Philosophical Society Held at Philadelphia for Promoting Useful Knowledge," an organization which includes natural scientists as well as social scientists and humanists. To determine what knowledge is useful Van Dyke assumes it should serve desirable purposes, it should be significant, and in particular it should be rational. On the latter point he quotes Dahl and Lindblom, "Any action is rational to the extent that it is 'correctly' designed to maximize goal achievement. . . . Given more than one goal (the usual human situation), an action is rational to the extent that it is correctly designed to maximize *net* goal achievement" (page 5). Thus for a political scientist "scholarship is significant when it contributes to the potential rationality of a political decision. Its significance varies with the importance of the end to which the decision relates, with the importance of the decision to the achievement of the end, and with the extent of the contribution to potential rationality" (page 5).

But beyond utility, significance, and rationality, the political scientist "should seek answers to questions or solutions to problems having to do with thought and action, ends and means, cause and effect, conditions and consequences. The study of politics should thus be conceived as a question posing and question answering activity" (page 6).

It is clear that Van Dyke's criteria have a large subjective element. He recognizes that in substance political science deals with values as well as with facts, with the "ought" as well as with the "is." His effort is to assist in the development of good scholarship in political science, not to reduce it to a "science" in the narrow sense. To this end he is concerned with qualitative distinctions such as those between facts and values, history and analysis, explanation and prediction, belief and knowledge, static and dynamic concepts. He also examines the methods of study which are suitable for determining the truth of statements in each of these categories.

Methods, Assumptions, Definitions

In the body of the book he examines critically certain key words which different political scientists have used in organizing their discipline—for example, conflict, power, interest group, decision making, and game playing. He asks the utility of each for the purpose intended. He does not discount the legal approach, though he warns against the "reifying" of law as something natural and beyond human control. He distinguishes descriptive from prescriptive law and discusses the value of mathematical expression in the former, with the remark: "It is a moot question whether Stalin's law or Parkinson's is the more valid" (page 82). He believes it unfortunate that political scientists do not know more about the methods of natural science than they do, but at the same time he recognizes that they must develop their methods from their own materials.

The book is doubtless in some degree stimulated by Walter Lippmann's comment which he quotes: "Nobody takes political science very seriously, for nobody is convinced that it is a science, or that it has any important bearing on politics" (page 204). The book may not allay this criticism, but it brings to light the underlying assumptions of leading political scientists and passes critical judgment on the methods they have used. It provides a body of definitions which will probably assist scholarship among the political scientists more than it will help either natural scientists or politicians to understand what contributions political scientists have made or can make. The latter are likely to ask, "Do political scientists have a technique that permits them to predict or control political phenomena better than the man in the street or the practiced politician?" Van Dyke does not answer this question. He says, "Whenever anyone makes a rational choice he is predicting" (page 42), that the capacity to explain past events correctly can help to predict future events, and that there is a difference between rational predictions and persuasive argument, although the latter,

if good enough, may be a self-confirming prediction. He outlines methods which have been used—analytical, inductive, deductive, comparative, "scientific"—but does not indicate whether any or all of them have actually produced reliable results of either practical or theoretical utility. The book is, as the title indicates, a philosophical analysis rather than an exposition of scientific method in the field of politics. It has a good index, gives access to recent literature in the field, and should be useful to political scientists; it will at the same time give natural scientists some insight into the way political scientists think.

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Hybrid Flora

Flora of New Zealand. vol. 1. *Indigenous Tracheophyta: Psilopsida, Lycopsida, Filicopsida, Gymnospermae, Dicotyledones*. H. H. Allan (deceased 29 October 1957). Government Printer, Wellington, 1961. liv + 1085 pp. Illus. $14.70.

This excellent volume, an original work, is nevertheless a lineal descendant of Cheeseman's *Manual* (1906; rev. ed., 1925). The unavailability of the latter, to bend a phrase from Cheeseman's preface in the first edition, "has long been a serious hindrance to the study of the indigenous vegetation, and a bar to inquiries of any kind connected therewith."

The long-awaited *Flora* was written by the late H. H. Allan, ably assisted by Lucy B. Moore, who completed the work. Compact owing to the use of thin paper, the book contains abundant dichotomous keys and descriptions of 116 families, 290 genera, 1457 species, and 272 varieties. Synonymy, distribution, and often critical notes are provided for each taxon; the numerous invaluable discussions of hybridism, polymorphism, and plasticity are tempting invitations to further study. All measurements are metric. In addition there are a chronological account of plant-taxonomic research in New Zealand from 1769 to 1958, a brief account of ecological and floristic conditions, a list of author abbreviations and dates, and a glossary of Maori plant names.

An estimated 80 percent of the species and 40 genera are endemic; 40 other genera but few identical species occur also in Australia. New Zealand offers a natural laboratory for the study of hybridization largely resulting from human disturbance. Most of the larger genera are suspected of having been affected, and some described varieties may owe their existence to this phenomenon.

A North American is struck by the fact that the families with most genera are Compositae, Umbelliferae, Scrophulariaceae, Papilionaceae, and Cruciferae. Among the largest genera are *Epilobium, Ranunculus, Senecio, Myosotis,* and *Gentiana*. Problems of bipolar distribution at once come to mind.

Of especial interest is the subantarctic element in the flora: "a whole vegetation type may be said to show 'disjunct' distribution across the South Pacific. . . . The acceptance of an evolutionary hypothesis forces one also to accept that the ancestors of these now widely separated plants . . . were once in genetic, if not geographical, contact. The biogeographer's task is to explain how this contact was achieved, and how it gave rise to the present pattern of distribution" [M. Holdgate in *New Scientist* **10**, 636 (1961)].

Exploration of these and many other problems will be greatly aided by the timely appearance of the *Flora*. The New Zealand Department of Scientific and Industrial Research, which sponsored the preparation and publication of the work, deserves congratulations.

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Moon Maps

Orthographic Atlas of the Moon. Supplement 1 to the *Photographic Lunar Atlas*. (Contributions, Lunar and Planetary Laboratory, No. 1). Compiled by D. W. G. Arthur and E. A. Whitaker. Gerard P. Kuiper, Ed. University of Arizona Press, Tucson, 1960.

The *Orthographic Atlas* is a very useful tool to be used in conjunction with the magnificent *Lunar Atlas* which was reviewed in the 29 July 1960 issue of *Science*. It is Supplement 1 of the *Lunar Atlas* and has been issued in two editions: (i) Edition A, on a high-grade coated paper, showing only the standard othographic grid and (ii) Edition B, on a washable, tear-resistant, heavy-duty, coated plastic showing, in addition to the orthographic grid, a latitude-longitude grid overprinted in blue, spaced by 2-degree intervals, giving approximate selenocentric coordinates. Edition B will be useful when the charts are to be used regularly at the telescope. The review copy is Edition A.

The supplement is being published in two parts. Part 1, "The Central Area of the Moon," is the portion now available. Part 2, covering the limb regions of the moon, has been announced for publication in the near future. The hard cover binder supplied with Part 1 will also accomomodate Part 2.

D. W. G. Arthur and E. A. Whitaker are skilled cartographers with expert knowledge of the lunar literature and of the problems of lunar cartography. They worked in close collaboration with the Aeronautical Chart and Information Center (ACIC) at St. Louis.

The grid lines shown on the maps have an interval of 0.01 lunar radius. They correspond to the intersects with the lunar surface of two sets of parallel planes, normal to each other, one set being parallel to the plane of the lunar equator and the other to the plane of the prime meridian. The point (0.0) corresponds to the center of the lunar disk as seen at zero libration in both latitude and longitude. The distance between consecutive grid lines at the center of the lunar disk is 10.8 miles or 17.4 kilometers.

Lohrmann (1824), Mädler (1837), and Schmidt (1878) produced remarkably accurate charts of the lunar surface before the advent of effective lunar photography. After 1900 it was possible to base lunar maps on the photographic triangulations of Franz and Saunder. Their triangulations were about 10 times more accurate than the prephotographic positions used by Schmidt and his predecessors. The present atlas is based on more control points than the work of Franz and Saunder, and for that reason it achieves much greater accuracy.

Two government agencies provided financial support: the National Aeronautics and Space Administration and the Geophysics Research Directorate, Air Force Cambridge Research Laboratories.

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Biological Units

The Cell. Biochemistry, physiology, morphology. vol. 4 and vol. 5, *Specialized Cells*, pt. 1 and pt. 2. Jean Brachet and Alfred E. Mirsky, Eds. Academic Press, New York. vol. 4, 1960. xv + 511 pp. vol. 5, 1961. xv + 597 pp. $20.

With these two volumes, covering more than a thousand pages, *The Cell* is well on its way. The middle volumes (2 and 3) are yet to come. There is no doubt that this is, and will remain for many years, a most important series of books and a necessity for any comprehensive biological library. There is no other collection of reviews on cell biology which covers this wide field with such thoroughness and quality.

Specialized cells are the subject of the 15 articles, which begin at the bottom of the scale with short, clear reviews on viruses by Thomas and on ciliates by Nanney and Rudzinska. Bacterial cytology, both with the light and the electron microscope, is dealt with by Robinow and illustrated by some beautiful photographs. Here one can well add a word of congratulation to the publisher on the quality of both the illustrations and the printing. Trager has written a most interesting article on intracellular parasites and symbionts—a subject which many cell biologists should know more about. One wonders, for example, how many of us are aware that the body louse appears to get vitamins from bacteria living as intracellular symbionts in a specialized organ.

Most of the reviews are concerned with the specialized tissue cells of the Metazoa—neurons by Hyden, photoreceptors by Miller, muscles by Huxley, glands by Gabe and Arvy, kidney by Forster, blood by Bessis, bone and cartilage by Lacroix, skin by Montagna, and antibody production by McMaster. Taken together, these reviews give an impressive survey of the differentiated cells of higher animals, and many of the articles deal with the physiology of the systems as well as with the morphology. But it is still striking how much less is known about cellular function than about cellular structure. In the same way that we still do not know what half of the organelles do within a typical cell, so also are we ignorant of the functions of many cell types within organs.

The last two articles deal with cancer cells. This is not an easy subject to review since much of the work on trying to differentiate tumor cells from normal cells has led to negative results. Oberling and Bernhard conclude that there is no "single morphological sign which is truly specific of cancer cells." But it is still possible to feel that more stress might have been laid on comparing cancer cells with other *growing* cells rather than with nongrowing cells of the tissue of origin.

Since *The Cell* is claimed by the publisher to be an "encyclopedic reference work," it is fair to point out that there are a number of omissions. Two of the commonest types of animal cells used in current research, gametes and amebas, are not included. Nor is there anything about plant cells, either at the level of the differentiated cells of higher plants or at the level of the cells of the lower groups, algae and yeasts.

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Essays on Genius

Some Reflections on Genius and Other Essays. Russell Brain. Lippincott, Philadelphia, 1961. 191 pp. $4.50.

Some Reflections on Genius consists of a selection of interesting essays—an initial one, from which the book derives its major title, plus 11 others that form commentaries on the lives of six men who distinguished themselves in ways that are related to the author's concept of genius. The commentary on Dr. Johnson is by far the longest, consisting of six essays. The book ends with two essays, one on symbols and images, the second on words.

In the first essay, which is the heart of the book, Russell Brain suggests that genius depends on the organization of the nervous system. He pays no more attention to the nervous system until the last two chapters, wherein he relates neurology to perception and the hemispheres of the brain to handedness and speech.

Intelligence is considered to be the most important general determinant of genius. Coupled with other specific independent abilities, it determines the character of genius. The connection between abnormality and genius is discussed in the first essay. Brain concludes that most geniuses are perfectly sane but that they tend to be emotionally unstable.

In the remaining essays the author interprets the lives of various great men and illustrates some aspects of his concept of genius.

The book suffers from disconnectedness. Had the commentaries been edited more carefully so as explicitly to illustrate the author's concept of genius, the book would have been more coherent and convincing.

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Wave Propagation

Wave Propagation in a Turbulent Medium. V. I. Tatarski. Translated by R. A. Silverman. McGraw-Hill, New York, 1961. 285 pp. Illus. $9.75.

Russian contributions to the theory of wave propagation in inhomogeneous media have been both extensive and impressive. An approach which has been consistently explored in the development of this theory is the combination of first-order perturbation theory, on the assumption of small inhomogeneities, combined with the Born, or far-field, approximation. In this book known results concerning the spectra of homogeneous turbulence are combined with these other approximations to yield a theory which gives impressive agreement with experimental data.

Tatarski gives a thorough account of the theory which results from the assumption of the validity of a perturbation approach, as well as the converse case which is amenable to analysis by the Wentzel-Kramers-Brillouin approximation. Applications are discussed in the fields of acoustic, electromagnetic, and optical propagation phenomena. The theory developed is amply documented by experimental data from studies of atmospheric turbulence and from the propagation of light and sound near the earth. Further reports are made of observations of twinkling and quivering of stellar images in telescopes, together with a theoretical interpretation along lines laid down earlier in the book.

This volume, together with the companion volume, *Wave Propagation in a Random Medium* (by Chernov), forms an important contribution to the literature because of the generality and wide applicability of the theories. American and British readers might, however, be

put off by statements in the first chapters which imply that the only significant contributions to the theory of turbulence have been made by Russian workers. Aside from this slight flaw, the book is an invaluable introduction to the field. The translation is readable both from the language and technical points of view.

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Space Travel Problems

Human Factors in Jet and Space Travel. A medical-psychological analysis. S. B. Sells and Charles A. Berry, Eds. Ronald, New York, 1961. xvi + 386 pp. Illus. $12.

The objective of this book is to present a comprehensive view of the human factors involved in operating high-performance aircraft and space vehicles. The material is well chosen to portray the joint effort of many disciplines, and it is presented in a clear, objective fashion. Although the lay reader may have difficulty with some sections, by and large those with a scientifically oriented background will find much of interest. The duplication of material, almost inevitable in a book written by 13 different authors, is very limited, and the style has a certain similarity and continuity throughout. Each chapter is well documented with factual information, and the book is relatively free of the flights of fancy so characteristic of some of the literature in the field of space exploration. There are selected bibliographies at the end of each chapter. The comprehensive subject index will be useful.

The content is primarily concerned with the human responses to the wide variety of stimuli encountered in flight at all altitudes. The medical and psychological problems of jet and space travel receive extensive treatment, but not out of proportion to their importance. The chapters range from the basic aspects of selection and skill of human operators to a detailed consideration of the tasks to be performed with safety and efficiency. Even the problems anticipated with group behavior, or the assemblage of several operators in a space vehicle, receive consideration. The area of radiobiology in space flight is analyzed extensively. The analysis of dysbarism, the symptoms resulting from evolved gases with extreme changes in pressure, constitutes an original and informative section. Preventive medicine and the control of contagious diseases are discussed, and the chapter on accidents is very informative. One of the most comprehensive chapters deals with cabin air conditioning, toxic exposures, decompression, radiation, acceleration, and noise. The engineered environment of the space vehicle, including the operational aspects of space flight, is carefully analyzed by well-qualified authorities.

In general, the book is an excellent introduction to the wide range of problems encountered thus far, and a forerunner in the area of the difficult problems remaining to be solved before travel, within and outside the earth's atmosphere, can be undertaken with safety and comfort.

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Russian Dictionary

Botanical Dictionary. Russian-English-German-French-Latin. Compiled by N. N. Davidov. F. Kh. Bakhteev, Ed. Foreign Language Scientific and Technical Dictionaries, Moscow, 1960. 335 pp. R 1.16.

Although many Russian botanical words, because of similarity to Western terms, can be translated easily by botanists who have a little familiarity with the language (beyond the alphabet) and even more words can be worked out by those who have some knowledge of the language and a little imagination, the remaining technical vocabulary bears little resemblance to its English-language counterpart and much of it is not found even in the best Russian-English dictionaries.

This botanical dictionary uses Russian as the basic language for the primary alphabetical listing and provides translations of the terms into four languages: English, German, French, and Latin. Each entry is numbered, and there are appended indexes to the four languages, which use the numerical system to locate the Russian equivalent in the main body of the work. Thus, the dictionary serves equally well for translating from the four languages into Russian. The 5806 entries are mostly in the area of gross morphology, so the dictionary will be of greatest use to plant taxonomists, anatomists, and morphologists. About 30 percent of the terms are plant names, translated into the vernacular in all languages except Latin, in which the binomial, author, and family are given. The translations of technical words are generally adequate, although frequently the English equivalents are unwieldy terms such as *dipyrenous, ramentaceous,* or *guttiflorous* which might better be translated into short descriptive phrases. There appear to be few factual errors; I find it difficult to believe that *bazidia* means *spore mother cell* as the dictionary indicates. The North American audience will object to the listing of *bergamot* as *Citrus bergamia* Risso, although this is in keeping with the Old World orientation of the dictionary terminology. *Sexless* is not the best English translation for *byezpolnii,* which is given better treatment as *geschlechtlos* and *asexuel* in German and French. Frequently, more than one equivalent is given so that some choice may be exercised in selecting the proper word. Occasionally, however, as in the choice of *rotten* or *corrupt* for *gniloi,* the user may decide upon another unlisted but more suitable word.

This dictionary will be of little use to botanists working outside the areas mentioned above, despite its title. Nevertheless, once its limitations are recognized, the dictionary will be useful to some botanists who have a minimal knowledge of Russian, and it can even be used by those who have no knowledge of the language. A comprehensive botanical, or better yet, biological Russian-English dictionary aimed at an English-speaking audience is desperately needed, but until such a dictionary is published this one will fill part of the existing vacuum.

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Anticipated Trend

Immunochemical Approaches to Problems in Microbiology. Michael Heidelberger and Otto J. Plescia, Eds. Rutgers University Press, New Brunswick, N.J., 1961. x + 402 pp.

It is probably safe to predict that in this next decade immunochemistry will be adapted to even more investigational pursuits in microbiology than during its entire first 50 years. Microbiology itself

has been enlarged to include nearly every aspect of biological and biochemical research. As attention is focused continually downward into the microscopic and submicroscopic world in attempts to define and resolve the nuances of biological function, the sensitivity and discriminatory power of the immunochemical discipline, methods, and techniques will find continually wider application.

Perhaps in anticipation of this trend, Heidelberger and Plescia assembled a notable international body of panelists. Five panels were organized to present and discuss recent advances in the quantitative aspects of specificity, multiplicity of bacterial antigens, immunochemistry of viruses, "non-specific" immunity, and the biosynthesis of antigens and antibodies. In this *Proceedings* volume, the comments made during the open discussions are published following the formal presentations of each panel; more frequently than not, those discussions emerge just as meaty and thoughtful as the prepared manuscripts.

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New Books

Biological and Medical Sciences

Advances in Protein Chemistry. vol. 15. C. B. Anfinsen, Jr., Kenneth Bailey, M. L. Anson, and John T. Edsall, Eds. Academic Press, New York, 1960. 457 pp. Illus. $13.

Biology. Relis B. Brown. Heath, Boston, Mass., ed. 2, 1961. 666 pp. Illus.

Biology through Microbes. A laboratory guide. Alfred S. Sussman. Univ. of Michigan Press, Ann Arbor, 1961. 202 pp. Illus.

Blood and Other Body Fluids. Analysis and compilations by Philip L. Altman. Dorothy S. Dittmer, Ed. Federation of American Societies for Experimental Biology, Washington, D.C., 1961. 557 pp. $10. A continuation of the handbook series prepared under the auspices of the National Acad. of Sciences–National Research Council.

Blood Platelets. Shirley A. Johnson, Raymond W. Monto, John W. Rebuck, and Robert C. Horn, Jr., Eds. Little, Brown, Boston, Mass., 1961. 755 pp. Illus. $18.50. Proceedings, 10th Henry Ford Hospital Symposia, held in March 1960.

Chemicals in Your Food and in Farm Produce. Their harmful effects. Franklin Bicknell. Emerson Books, New York, 1961. 192 pp. $2.95.

Elementary Human Physiology. A text for undergraduates. Terence A. Rogers. Wiley, New York, 1961. 429 pp. Illus. $6.50.

Experimental Immunochemistry. Elvin A. Kabat and Manfred M. Mayer. Thomas, Springfield, Ill., ed. 2, 1961. 917 pp. Illus. $26.50.

Microbial Cell Walls. M. R. J. Salton. Wiley, New York, 1960. 103 pp. Illus. $3.50. 1960 CIBA lectures in microbial biochemistry, presented at Rutgers University.

Microbial Reaction to Environment. Eleventh symposium of the Society for General Microbiology. Cambridge Univ. Press, New York, 1961. 426 pp. Illus. + plates. $7.50.

Progress in Biophysics and Biophysical Chemistry. vol. 11. J. A. V. Butler, B. Katz, and R. E. Zirkle, Eds. Pergamon Press, New York, 1961. 282 pp. Illus. $12.50.

Protides of the Biological Fluids. H. Peeters, Ed. Elsevier, Amsterdam, Netherlands, 1961 (order from Van Nostrand, Princeton, N.J.). 366 pp. Illus. $16.75. Proceedings of the colloquium held in Bruges, Belgium, in 1960.

Economics and Social Sciences

The Dynamics of Communism in Eastern Europe. R. V. Burks, Princeton Univ. Press, Princeton, N.J., 1961. 256 pp. Illus. $5.

Economics. An introductory analysis. Paul A. Samuelson. McGraw-Hill, New York, ed. 5, 1961. 863 pp. Illus. $7.50.

The Lolo of Liang Shan (Liang-shan I-chia). Lin Yueh-hua. Translated by Ju-Shu Pan. Wu-Chi Liu, Ed. HRAF Press, New Haven, Conn., 1961 (order from Taplinger, New York). 167 pp. Illus. $3.

Measurement and Evaluation in Psychology and Education. Robert L. Thorndike and Elizabeth Hagen. Wiley, New York, ed. 2, 1961. 610 pp. Illus.

Tristes Tropiques. C. Levi-Strauss. Translated by John Russell. Criterion Books, New York, 1961. 404 pp. Illus. + plates. $12.50.

General

Arms Control, Disarmament, and National Security. Donald G. Brennan, Ed. Braziller, New York, 1961. 475 pp. $6.

Careers and Opportunities in Physics. Philip Pollack. Dutton, ed. 2, New York, 1961. 159 pp. Illus. $3.75.

The Forbidden Voyage. Earle Reynolds. McKay, New York, 1961. 281 pp. Illus. $4.95.

Human Heredity. Jean Rostand (Translated by Wade Baskin from *L'Heredité Humaine*). Philosophical Library, New York, 1961. 139 pp. $4.75.

A Prelude to Medical History. Félix Martí-Ibãnez. MD Publications, New York, 1961. 277 pp. Illus. $5.75.

Scientific Russian Guide. Handbook for students and professionals interested in scientific Russian. Mary A. Emery and Serge A. Emery. McGraw-Hill, New York, 1961. 198 pp. $4.50.

Mathematics, Physical Sciences, and Engineering

Abundance of Chemical Elements. V. V. Cherdyntsev. Translated by Walter Nichiporuk. Univ. of Chicago Press, Chicago, Ill., 1961. 324 pp. Illus. $10.

Advanced Calculus. An Introduction to analysis. Watson Fulks. Wiley, New York, 1961. 536 pp. Illus. $11.25.

Astronautics. Fundamentals of dynamical astronomy and space flight. Arthur I. Berman. Wiley, New York, 1961. 365 pp. Illus. $9.25.

Chemistry. Michell J. Sienko and Robert A. Plane. McGraw-Hill, New York, ed. 2, 1961. 636 pp. Illus.

Codes for Reactor Computations. International Atomic Energy Agency, Vienna, Austria, 1961 (order from International Publications, New York 22). 538 pp. Illus. $8. Proceedings of the symposium held in April 1960.

College Algebra. Paul K. Rees and Fred W. Sparks. McGraw-Hill, New York, ed. 4, 1961. 442 pp. Illus. $6.50.

Design and Construction of Ports and Marine Structures. Alonzo DeF. Quinn. McGraw-Hill, New York, 1961. 539 pp. Illus. $16.

Electronic Packaging with Resins. A practical guide for materials and manufacturing techniques. Charles A. Harper. McGraw-Hill, New York, 1961. 351 pp. Illus. $11.

Flammenphotometrie. R. Herrmann and C. Th. J. Alkemade. Springer, Berlin, 1960. 402 pp. Illus. + plates. DM. 88.

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Reports

Inactivation by Ultraviolet Light of an Acriflavine-Sensitive Gene Function in Phage T4D

Abstract. Mutants of phage T4D can be isolated which multiply in the presence of concentrations of acriflavine inhibitory to the growth of wild-type phage. Bacteria mixedly infected with resistant and sensitive phage are unproductive in the presence of acriflavine. Irradiation of the sensitive phage with ultraviolet light results in inactivation of the function of the gene for acriflavine sensitivity, permitting the mixedly infected complexes to yield phage. This function is inactivated in an exponential manner and has a cross section comparable to cross sections of other gene functions in T4D.

Mutants of phage T4D can be isolated which are capable of normal growth in low concentrations of acriflavine (0.25 per milliliter of "acriflavine neutral" [Nutritional Biochemical Corporation]). Under the same conditions, few (0.001 to 0.0001 percent) bacteria infected with wild-type phage are able to produce any infective particles. Crosses have shown that the sites of 12 out of 12 independently isolated acriflavine-resistant (*ac*) mutants are all about six map units from a terminal marker in the *r*IIB cistron, and the order *r*IIA, *r*IIB, *ac* has been established. Only 0.1 to 1 percent of cells infected with equal numbers of *ac* and *ac*$^+$ phage produce any phage in the presence of acriflavine. Thus acriflavine sensitivity (*ac*$^+$) is "dominant" over acriflavine resistance (*ac*) in the sense that acriflavine inhibits phage production in cells mixedly infected with *ac* and *ac*$^+$ phage.

Krieg (*1*) has measured the ultraviolet-light cross section of the *r*IIA$^+$ and *r*IIB$^+$ gene functions of phage T4D. In his experiments, *Escherichia coli*, strain K12(λ), bacteria were mixedly infected with unirradiated *r*II phage and irradiated wild-type phage. Krieg found that the fraction of mixedly infected bacteria which produced any phage decreased in an exponential manner as a function of ultraviolet dose to the *r*$^+$ phage, but at a rate much less than the rate of loss of infectivity of the phage particle. From this and other observations it was concluded that mixedly infected bacteria cannot produce phage unless the *r*II$^+$ gene of the infecting wild-type phage is free of ultraviolet damage affecting its function. The properties of the *ac*-*ac*$^+$ system described above make it possible to obtain a similar estimate of the ultraviolet target size of the *ac*$^+$ function. In contrast to the properties of the *r*II system, however, bacteria mixedly infected with *ac* and *ac*$^+$ phage are productive in the presence of acriflavine only if the *ac*$^+$ gene function in the infecting wild-type phage has been *damaged* by ultraviolet. Thus, in principle, one could mixedly infect bacteria with unirradiated *ac* and irradiated *ac*$^+$ phage and measure the increase in the fraction of mixedly infected cells yielding phage in the presence of acriflavine as a function of ultraviolet dose. From this one would obtain a measure of the *inactivation* of the *ac*$^+$ function, rather than of its survival.

In order to control effectively the condition of mixed infection, our experimental design was somewhat more complicated, combining both the *ac* and *r*II systems. In addition to the *ac* alleles, an *r*IIA(*r*61) and an *r*IIB(*r*73) marker were employed in these experiments. K12(λ) bacteria were infected at low multiplicity (0.2 of each phage) with unirradiated *r*IIA*r*IIB$^+$*ac* phage and with *r*IIA$^+$*r*IIB*ac*$^+$ phage which had been exposed to various doses of ultraviolet light (from a General Electric 15-watt germicidal lamp). Only mixedly infected bacteria will yield phage, because both the *r*IIA$^+$ and the *r*IIB$^+$ functions are required for productive infection of K12(λ). Since the multiplicity of infection is low, the majority of productive complexes will have received only one phage of each genotype.

Samples of the mixedly infected bacteria were plated on the indicator strain S/6. Any complex which yields phage forms a plaque on S/6. Thus we measure the number of mixedly infected cells which received a phage with an undamaged *r*IIA$^+$ gene function. This number decreases with increasing dose, because of damages of all kinds—that is, damages preventing injection as well as those specifically inhibiting the *r*IIA$^+$ function. Samples were also plated on plates supplemented with acriflavine. Here we measure the number of mixedly infected bacteria which received a phage with an undamaged *r*IIA$^+$ gene *and* a damaged *ac*$^+$ gene. The difference between the number on supplemented and the number on unsupplemented plates is the number of complexes which received both an undam-

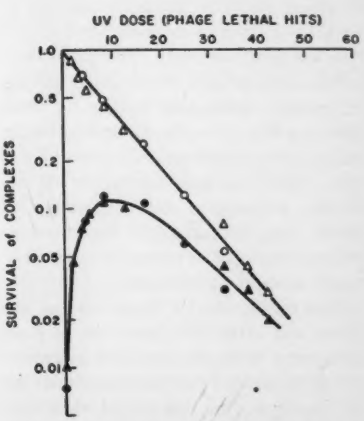

Fig. 1. Ultraviolet-light inactivation of infected bacteria plated with and without acriflavine. Strain K12(λ) bacteria infected with *r*IIA*r*IIB$^+$*ac* and ultraviolet-irradiated *r*IIA$^+$*r*IIB*ac*$^+$ phage are plated before lysis on plates seeded with S/6 (open symbols) and on plates seeded with S/6 and supplemented with acriflavine (solid symbols). Circles and triangles represent different experiments. The ordinate is the surviving fraction of plaque-forming infected bacteria relative to the plaque-formers at zero dose on unsupplemented plates. The abscissa is the dose expressed in phage lethal hits (*4*).

Instructions for preparing reports. Begin the report with an abstract of from 45 to 55 words. The abstract should *not* repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper.

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to *one* 2-column figure (that is, a figure whose width equals two columns of text) or to *one* 2-column table or to *two* 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to contributors" [*Science* **125**, 16 (1957)].

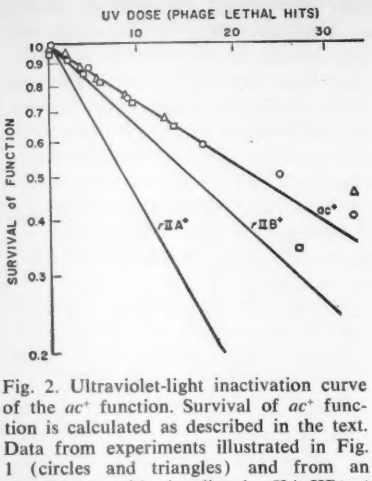

Fig. 2. Ultraviolet-light inactivation curve of the ac^+ function. Survival of ac^+ function is calculated as described in the text. Data from experiments illustrated in Fig. 1 (circles and triangles) and from an experiment with irradiated *r*IIA*r*IIB$^+ac^+$ and unirradiated *r*IIA$^+$*r*IIB*ac* (rectangles). Survival curves for the *r*IIA$^+$ and the *r*IIB$^+$ functions (obtained in these experiments) are shown for reference. For the ac^+ function, zero-dose values are less than 1, due to the small fraction of mixedly infected bacteria which form plaques in the presence of acriflavine (at zero dose).

aged *r*II$^+$ and an undamaged ac^+ gene. This number, divided by the number on unsupplemented plates, gives the fraction of complexes at each dose in which the ac^+ function survives *among* those in which the *r*IIA$^+$ function survives as well. Data from two experiments of this type are given in Fig. 1. The calculation of the data to give the survival of the ac^+ gene is presented in Fig. 2. Also given in Fig. 2 are comparable results from an experiment with unirradiated *r*IIA$^+$*r*IIB*ac* and irradiated *r*IIA*r*IIB$^+ac^+$. In this experiment the inactivation of the ac^+ function, together with the survival of the *r*IIB$^+$ rather than the *r*IIA$^+$ gene function, is measured.

Our results on the target sizes of the *r*IIA$^+$ and *r*IIB$^+$ functions are in good agreement with the previous measurements by Krieg (*1*). The survival of the ac^+ function, like that of the *r*IIA$^+$ and *r*IIB$^+$ functions, decreases in a simple exponential manner with increasing irradiation dose. The slope of the survival curve indicates that the ac^+ function is 0.03 of the total ultraviolet-sensitive target of the phage. No data are available at the present time which will permit a comparison between the ultraviolet cross section of the ac^+ function and an estimate of the length of the ac^+ gene obtained from mapping experiments.

In the experiments described here we measure only the damage to the ac^+ genes among those phage in which the *r*II$^+$ function survives. Any class of damages which simultaneously inactivate both the ac^+ and one of the *r*II$^+$ genes is not included in our estimate of the *ac* target size. One class of damage which might be expected to occur is that which renders the phage totally inoperative (for example, that which prevents injection). However, Barricelli (*2*) has suggested that irradiation damages, although discretely localized in the genome, may have a finite size. If this were true one would expect that some ultraviolet hits of this type could inactivate two neighboring genes at once. Indeed, Krieg (*1*) found a correlation between the inactivation of the *r*IIA$^+$ and the *r*IIB$^+$ genes which could be explained on this basis. If such extended damages contributed significantly to our data, the apparent target size of the ac^+ gene would be smaller in experiments requiring survival of the *r*IIB$^+$ gene than in experiments requiring survival of the *r*IIA$^+$ gene. As can be seen from the data presented in Fig. 2, no such effect is detectable. This only means that, if ultraviolet-induced lesions have a finite size, this size must be smaller than the distance between the *r*IIB$^+$ gene and the ac^+ gene (less than six map units).

Features of this system may make it useful in other studies on the genetic effects of ultraviolet irradiation. Since the cells which yield phage are those in which the irradiated parent has received at least one ultraviolet-induced lesion, there exists a selective system for examining the genetic consequences of very low doses of ultraviolet light. Since only that fraction of the irradiated phage which has a surviving *r*II$^+$ function yields phage, experiments are not influenced by damages which render the page totally inoperative (*3*).

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17 April 1961

Nonreinforced Trial Procedure for Probability Learning

Abstract. For rats in a T-maze, nonreinforced trials were interspersed with reinforced trials to insure that .67 of all reinforcements would be dispensed on the more frequently reinforced side. At asymptote, the proportion of responses to the more frequently reinforced side was .67.

Probability learning (as defined here) refers to experiments in which each trial ends with one of two responses. One response (called *M* in this report) is more frequently reinforced than the other response (called *L*). The independent variable is the ratio of reinforcements for *M* to all reinforcements; this ratio is called π. The dependent variable is the proportion of trials during which *M* is emitted; this proportion is called *P*. Functional relationships between π and *P* have been derived from theories about the effect of reinforcements on response probability, and much probability learning experimentation has been devoted to the development of these theories (*1*, *2*). Unfortunately, all the procedures used to control π in animal learning situations involve the introduction of factors not considered in these theories. In the light of generally applicable behavior principles, these factors should affect *P* as follows.

1) In the *forced trial procedure*, forced trials are interspersed with free trials in order to control π, and *P* is reckoned as the proportion of free trials during which *M* is emitted. An extraneous factor is a discrimination between forced trials and free trials which develops in the course of the experiment, so that reinforcement of forced trials affects *P* less than does reinforcement of free trials (*3*).

2) In the *correction procedure*, one response is selected for reinforcement on each trial, *M* being selected with probability π. If the initial response of the trial is not the response to be reinforced, the trial does not end until the reinforced response is emitted (that is, "correction" is permitted). *P* is reckoned as the proportion of trials during which *M* is the initial response of the trial. One possible extraneous factor in this procedure is that an initial response not scheduled for reinforcement may receive delayed reinforcement because it is followed by reinforcement of a correction. In addition, a correction is topographically different from an initial response, so that a discrimination between corrections and initial responses

Table 1. P as a function of trials.

Trials	Mean of P	.05 Fiducial limits of mean
1–30	.593	.562–.624
31–60	.660	.625–.694
61–90	.672	.636–.708

may develop. For both of these reasons, reinforcement of corrections should not change P as much as reinforcement of initial responses. By the rules of the correction procedure, P of all reinforcements for M will follow initial responses; the corresponding proportion for L is $(1-P)$, since L is the initial response on $(1-P)$ of the trials. It is known (*2*) that after a few trials P becomes larger than .5, so that most of the M reinforcements follow initial responses, while most of the L reinforcements follow corrections.

For the above reasons, a new procedure, called the *nonreinforced trial procedure*, was devised. Only one response is allowed to occur on any one trial. Nonreinforced trials are interspersed with reinforced trials, so that π is controlled.

In the present experiment, 19 rats, deprived of food for approximately 22.5 hr, were subjected to one trial per day for 90 days in a slightly modified version of a T-maze described by Nunis (*4*). The nonreinforced trial procedure was used to reinforce a position preference with $\pi = .67$. Reinforcements were administered in blocks of three, consisting of two M reinforcements and one L reinforcement. At the beginning of a block, whichever response was made was reinforced. When all of the assigned reinforcements had been received for one of the two responses, that response was not reinforced until the assigned number of reinforcements had been obtained for the other response. It so happened that .608 of all trials were reinforced. (Reinforcement consisted of allowing the rat to enter a white goal box from a black alley to eat ground chow for 20 sec. When nonreinforcements were scheduled, a swinging door leading to the nonreinforced goal box was locked. Five seconds after the rat interrupted a photobeam 1.5 in. in front of this door, it was removed from the apparatus.)

Table 1 shows the mean of P during each 30-trial portion of the experiment and .05 fiducial limits for this mean (t-test). Toward the end of the experiment, P is approximately equal to π. Estes (*2*) has shown that asymptotic equality of P and π is implied by certain assumptions about the effect of reinforcement on response probability provided that all trials are reinforced. If our result is to confirm Estes' views, it must be shown that the nonreinforced trials do not affect P. Under the present use of the nonreinforced trial procedure, nonreinforcements of M can occur only during a block of reinforcements in which the two reinforcements of M have already occurred, but L has not yet occurred. The value of P on the trial following the second reinforcement of M during such a block is called Prr. If the trial following these two successive reinforcements of M also results in M, this last trial is not reinforced; the value of P after such a nonreinforcement is called $Prrn$. Similarly, the value of P following two such nonreinforcements is called $Prrnn$. These statistics were obtained for each rat and their means were: $Prr = .839$; $Prrn = .788$; and $Prrnn = .664$. This decrease in P as a function of nonreinforcement of M is significant at the .05 level (Kendall $W = .161$, 18 degrees of freedom), indicating that without special assumptions about the interaction of reinforcement and nonreinforcement, the present experiment, like previous probability learning experiments with animals, cannot decisively confirm or reject theories about the effect of reinforcement on response probability.

Important information about the role of the nonreinforcements in the nonreinforced trial procedure is supplied by two proportions, $F(M)$ and $F(L)$. $F(M)$ is the proportion of M occurrences which are reinforced:

$$F(M) = x_\pi / P$$

where x is the proportion of all trials (both M and L) which are reinforced (so that x_π is the proportion of all trials containing reinforced occurrences of M). Similarly, $F(L)$ is the proportion of L occurrences which are reinforced:

$$F(L) = x\,(1-\pi)/(1-P)$$

It may be verified that when $P < \pi$, $F(M) > F(L)$; that when $P = \pi$, $F(M) = F(L)$; and that when $P > \pi$, $F(M) < F(L)$. I have not been able to relate these mathematically derived facts to the above-mentioned theories (*1*, *2*) in any rigorous way. However, if it is assumed that when $F(M) > F(L)$, P increases, and that when $F(M) < F(L)$, P decreases, these facts imply that once P reaches π, it will oscillate around π. (The possibility that P will remain constant at π is ignored because it was empirically shown that $Prr > \pi$.) Presumably, then, the mean of P will approximate π (*5*).

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20 March 1961

Hemorrhage in a Coccinellid Beetle and Its Repellent Effect on Ants

Abstract. Special refinements of the bleeding mechanism of the Mexican bean beetle, *Epilachna varivestis* Mulsant, are described, and the defensive effectiveness of the mechanism against ants is demonstrated. Ants may have provided a major selective force in the evolution of the mechanism.

A variety of insects and other terrestrial arthropods have the peculiar habit of discharging small droplets of blood from one or more points on their body surface when they are handled or otherwise molested. This autohemorrhage or "reflex bleeding" as it is often called, is generally acknowledged to be a mechanism of defense against predators. The purpose of this report (*1*) is to describe some hitherto unnoticed adaptive features of this mechanism as it occurs in adults and larvae of the Mexican bean beetle, *Epilachna varivestis* Mulsant.

In adult *Epilachna*, as in apparently all coccinellid beetles that show reflex bleeding, the release of blood is exclusively from the tibio-femoral joints of the legs (*2*). In order to facilitate observation of the bleeding response, individual beetles were affixed to rods [by a technique used previously with other insects and described elsewhere (*3*)], and were subjected to localized traumatic stimuli, applied either by pinching individual appendages with forceps, or by touching different body

regions and the elytra with the point of a hot needle. Bleeding was the almost invariable response: the only stimuli which were ineffective were those applied to the dorsum of the abdomen beneath the elytra (this is, of course, a region not likely to be initially traumatized by a predator).

Of special interest was the finding that the legs do not all bleed simultaneously, but do so individually (Figs. 1–4). As a rule, only the particular leg closest to the stimulus responds at a given time (Figs. 5–8). The leg is even sometimes rotated in such a way that its blood-laden knee joint is brought closest to the point traumatized (for example, Fig. 6). When stimuli are repeatedly applied to the same site, there occurs first an enlargement of the initial drop formed on the nearest leg, followed by a spread of the bleeding response to other legs, first to those of the same side and then to those of the opposite side. The droplets sometimes flow onto the lateroventral margins of the body; in ambulatory specimens this is a common consequence of leg movements.

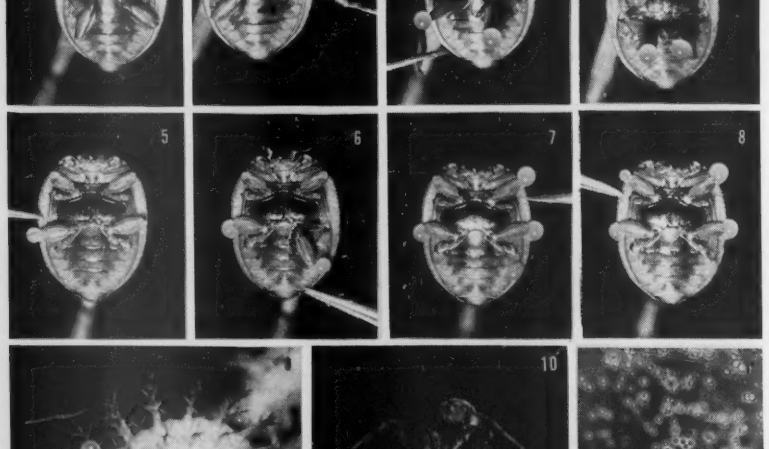
Simultaneous application of several localized stimuli results in a synchronous discharge from a corresponding number of legs, involving invariably only those closest to each stimulus. Broadly generalized stimulation, as when the animals are handled, results in simultaneous or almost simultaneous discharge from all six legs. The blood coagulates rapidly on exposure to air, hardening to a crust within minutes. The crust does not hinder the beetle in any apparent way, and eventually always flakes off completely during the normal course of activity.

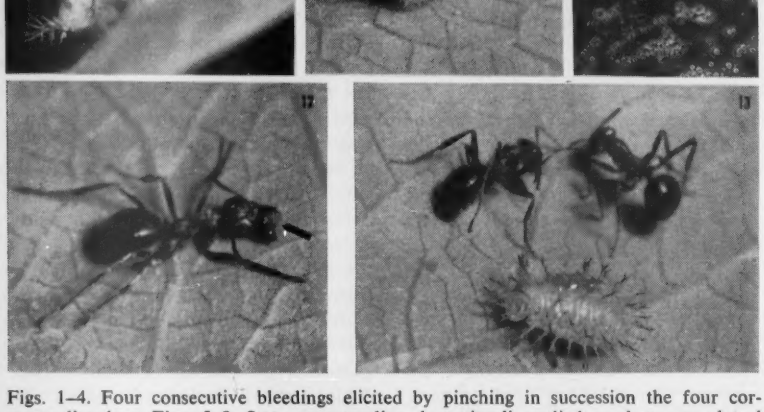
The amount of blood that the beetles can stand losing is considerable; no noticeable ill effects result from a loss of six droplets, one from each leg. Some of our beetles did eventually die, but this may well have been due to the more or less extensive cautery induced by the hot needle.

In the larvae of *Epilachna*, bleeding is also easily induced, but it cannot be considered autohemorrhagic in a strict sense, since it occurs only at the actual sites of injury. The entire back and sides of the soft-bodied larva are beset with a dense armature of erect branched spines. These spines are hollow and brittle, and when prodded rupture readily, resulting in instantaneous emergence of a small droplet of blood at the break (Fig. 9). Like the adults, the larvae can also survive considerable hemorrhage: specimens that were shorn of all their spines went on to pupate normally.

The distasteful properties of a variety of coccinellid beetles have been demonstrated, at least with regard to some vertebrate predators (*4*). The localized nature of the bleeding response suggests that it might also serve with particular effect against smaller arthropod predators that are likely to inflict local rather than general injury when they first attack. Observations on arthropod predators are rare, however, and such as do exist are sketchy at best (*5*). This prompted us to set up a series of laboratory encounters between adults and larvae of *Epilachna* and the ant *Formica exsectoides* Forel.

The adult beetles were introduced directly into an artificial nest of the ants; they were attacked instantly, the ants converging upon them in groups, and biting them. Sometimes the beetles were seized by an appendage, but more





Figs. 1–4. Four consecutive bleedings elicited by pinching in succession the four corresponding legs. Figs. 5–8. Same as preceding, but stimuli applied as shown to elytral and abdominal margins. Fig. 9. Two droplets of blood (arrow to smaller drop) oozing from ruptured larval spines. Fig. 10. *Formica* worker about to bite and rupture larval spines. Fig. 11. Smear of blood released at knee joint of adult (phase contrast). Fig. 12. *Formica*, after attack on larva, dragging its body and blood-laden mouth parts (arrow). Fig. 13. Two ants, contaminated with larval blood, stuck together by their antennae.

frequently—since they "feigned death" and tucked their legs under the body—they were grasped by the elytral margins. No sooner had an ant bitten than the beetle responded by bleeding from the nearest knee joint. The droplet of blood invariably spread onto the assailant, contaminating its antennae, and usually oozing between the gaping mouthparts. The ant immediately released its hold, backed away abruptly, and then began intensive cleansing activities, brushing its antennae with the forelegs, or walking along slowly, flailing its legs and dragging its blood-drenched mouth parts along the substrate (Fig. 12). [This peculiar dragging behavior has been noticed before in this ant in comparable encounters involving arthropods with defensive secretions (*6*)].

More pronounced signs of distress became apparent as the blood coagulated, becoming increasingly viscous and sticky. It was then not uncommon to see an ant with its antennae stuck together, with a leg stuck to an antenna, or with the mouth parts gummed up and virtually immobilized. Groups of ants would become stuck to one another (Fig. 13). Recovery is eventually always complete, but it may take an ant several minutes to over an hour to clear itself from the remaining flakes of clot. A few tests were also made by releasing ants and beetles onto the leaves of the beetle's food plant. The results differed only in that they pointed out clearly the protective value of "death-feigning"; when attacked, the beetles often simply let themselves drop from the leaves.

The experiments with larvae were all done on leaves. The ants attempted to bite, but would usually only succeed in breaking one or more of the larval spines. The droplets of blood released were instantly repellent to the ants, and affected them in the same way as did the blood of the adults. Unlike the adults, the larvae never dropped from leaves.

Evidently, the bleeding mechanism of *Epilachna* is a means of defense admirably suited for use against ants. It is certainly conceivable that the mechanism might be similarly effective against other arthropod enemies, but ants may well be one of the most important groups of predators—if not *the* most important group—responsible for the evolution of the mechanism. Most coccinellids are carnivorous, and the habit shared by so many of them of feeding on aphids and coccids may well be primitive for the family (*7*). Though the tribe to which *Epilachna* belongs (Epilachnini) is predominantly herbivorous, it is "regarded as a relatively late and specialized offshoot of the Coccinellid stock . . ." (*8*). It seems that its hemorrhagic defense mechanism is an evolutionary legacy from its Homoptera-feeding forebears, whose exposure to the well-known aggressive tendencies of Homoptera-tending ants (*9*) provided the selective force that evoked the adaptation in the first place. It is interesting in this connection to note that the larvae of certain lycaenid butterflies that also feed on Homoptera tended by ants are protected from attack by secreting a substance that is not repellent but attractive to the ants (*10*).

In the past there has been some controversy as to whether the liquid exudate of adult coccinellids is indeed blood, rather than the product of special glands (*11*). Our own observations tend to confirm the prevalent view that it is blood. The liquid has all the diagnostic features of blood (Fig. 12): the same cells are present, and so are the tiny spherules known to be typical of coccinellid blood (*12*). One might add also that the size of the droplet released at the knee joint often distinctly exceeds the estimated volume of the leg that produces it. Histological studies (*13*) reveal no glandular reservoirs of appropriate capacity.

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17 April 1961

Localization of Porphyrin Fluorescence in Planarians

Abstract. Two species of planarians were studied by fluorescence microscopy. Red fluorescence of uroporphyrin was observed localized in the epidermal rhabdites and subepidermal rhabdite-containing gland cells. Fluorescence was observed in isolated rhabdites of homogenates, but was not seen in rhabdites of the living animal. The identity of rhabdites was established by their location, shape, size, and acidophilic staining properties.

The occurrence of uroporphyrin in the planarian, *Dugesia dorotocephala*, has been described previously (*1*). This finding was based on analyses of acid extracts of the planarian. In that study, general porphyrin fluorescence of the acid-treated animal was observed; in the present study, however, higher intensity of ultraviolet light permitted the observation of fluorescence within definite morphological structures.

Detection of fluorescence was made microscopically; a Leitz HB 200 lamp was the source of ultraviolet light. A Leitz 2-mm BG-12 exciter filter was used, and a 2.5-mm OG-1 barrier filter was placed in the ocular. Observations and photographs were made with a dark-field condenser.

The two species of planarians studied were *Dugesia dorotocephala* and *D. tigrina*. Living animals were placed in water between a slide and cover slip, and exposed to ultraviolet light under the microscope. Red fluorescence observed in the living animal was restricted to a few irregular structures within cells lining the digestive tract, which probably were food particles or products of digestion. However, after treatment with a variety of chemical substances, a brilliant and extensive red fluorescence was observed in the epidermis and subepidermis of these animals.

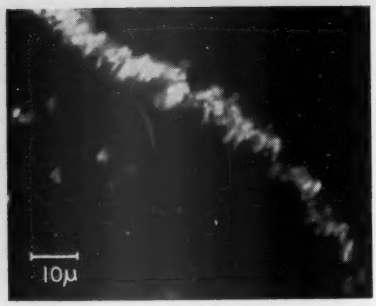

Fig. 1. Cross section of *Dugesia dorotocephala* showing fluorescence of epidermal rhabdites and subepidermal rhabdite clusters. The preparation was from an animal fixed in 100-percent ethyl alcohol; it was cleared and embedded in paraffin and sectioned at 5 μ. The section was then deparaffinized and mounted in nonfluorescing immersion oil for observation under the fluorescence microscope.

The substances used were 95-percent ethyl alcohol, 5-percent neutral formalin, 0.05*N* NaOH, 0.1*N* NH_4OH, and 50-percent H_2O_2. The appearance of fluorescence seemed to coincide with death of the animal. Observation was facilitated by applying pressure on the cover slip and flattening the animal. The red fluorescence was localized within rod- or crescent-shaped structures at the surface and just below the surface of the epidermis. The identification of these structures as rhabdites was based on their location, shape, and size (*2*). Their length varied from 2 to 8 μ, and their width from 1 to 3 μ. These structures could be seen as refractive bodies in the epidermis of the living animal under the phase-contrast microscope. The identity of the rhabdites was further checked by observing fluorescent rhabdites in acetone-frozen and dried sections, and in sections of animals fixed in 100-percent ethyl alcohol, cleared in benzene, and embedded in paraffin. Although some porphyrin may have been extracted by the alcohol, deparaffinized sections under the microscope clearly revealed fluorescent rhabdites perpendicular to the surface of the animal (Fig. 1). In the subepidermis, rhabdites were noted in clusters, which were identified as rhabdite-forming gland cells. Fluorescent rhabdites were retained in a saccular gland cell when the whole animal was placed in 0.05*N* NaOH; the cells separated and flowed freely when slight pressure was placed upon the cover slip. This treatment allowed observation of the number and shape of rhabdites within the somewhat swollen gland cells (Fig. 2).

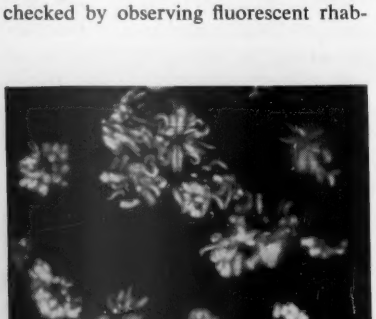

Fig. 2. Cluster of fluorescing rhabdites within gland cells of *Dugesia tigrina* from a squash of the whole animal treated with 0.05*N* NaOH, and observed under the fluorescence microscope.

Sections were stained with acid dyes such as eosin, orange G, picric acid, and fast green. The rod-shaped structures which exhibited the red fluorescence also showed the marked eosinophilia and acidophilia described by other investigators as characteristic of rhabdites (*3*, *4*). Rhabdites did not stain with basic dyes, such as methylene blue and toluidine blue.

Homogenates of planarians were made in a Potter homogenizer, and a drop of homogenate was examined under the fluorescence miscroscope. Red fluorescence was clearly visible in rhabdites isolated from other cellular materials. Fluorescence was also visible in clusters of rhabdites and in some smaller "subrhabdite" units, which may be structural precursors of rhabdites. These "subrhabdites" could also be observed within some gland cells after treatment with 0.05*N* NaOH. The fluorescence of the rhabdites in the homogenate appeared without any chemical pretreatment of the homogenate. When homogenates or whole planarians were subjected to HCl (1*N* or 2.5*N*), an extraction of red fluorescing material occurred. Examination under the microscope revealed an extraction of fluorescence from the rhabdites. The acid extract contained uroporphyrin as analyzed by the paper chromatography method of Nicholas and Rimington (*5*).

Rhabdites were observed to stain intensely with bromphenol blue, indicating protein in rhabdites; this confirmed observations of Prenant (*3*) and Pedersen (*4*) made on several other species of planarians. A linkage between protein and uroporphyrin or between a metal and uroporphyrin may account for the lack of fluorescence in the rhabdites of living animals. Such a linkage would eliminate the alternating double-bond structure upon which the fluorescence of porphyrin depends. On the other hand, the uroporphyrin may be present as a nonfluorescing porphyrinogen (*6*).

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13 April 1961

Aging in Irradiated and Nonirradiated Hydras

Abstract. Evidence is presented that as hydras become older they bud more slowly and become more susceptible to adverse conditions. In these studies, a 2000-roentgen dose of x-radiation did not seem to affect the rate of these changes. The mean number of tentacles did not change with age.

It has been suggested by Brien (*1*) that individual hydras are theoretically immortal. He bases this suggestion on the fact that there seems to be no noticeable decrease in the budding rate of individuals maintained under observation for long periods (*2*). Also, in each individual hydra there is a continual replacement of the entire cell population (*1*, *3*), and it may be that this produces a continual rejuvenescence. The facts that stimulation of the rate of cellular replacement by repeated injury seems to increase the

Table 1. Number of buds produced by offspring minus the number produced by parents ($\bar{x}$)

Group	Generation	$\bar{x}$	t	p
Control	4	−0.06	0.20	0.8
Control	8	.42	1.56	.07
Control	12	.63	3.07	< .005
Irradiated	4	.54	1.1	.15
Irradiated	8	.765	1.88	< .05
Irradiated	12	.53	1.59	.07

Table 2. Number of buds produced by irradiated hydras minus number of buds produced by controls ($\bar{x}$).

Group	Generation	$\bar{x}$	t	p
Parents	4	0.10	0.28	0.7
Parents	8	−0.24	.65	.5
Parents	12	.14	.47	.65
Buds	4	.50	1.37	.2
Buds	8	.20	0.79	.2
Buds	12	.06	.155	.9

resistance of hydras to adverse conditions (*4*) and that interstitial cells from a normal hydra can restore an irradiated one (*5*) support the notion of rejuvenescence.

However, several investigators have argued that aging does take place in *Hydra*. Hase and Grosz (*6*) found that the number of tentacles increases with age; Vishnevs'kii (*7*) found that the time required for successive buds to develop increases with age; and Hyman (*8*) noticed that both irregular budding and depression occur more readily in older individuals. Hase reported populations of *Hydra oligactis* and *H. vulgaris* that lived only 167 and 337 days, respectively. However, Pearl and Miner (*9*) examined Hase's data and found that the death rate was constant with increasing age. Therefore, death was probably due to environmental accidents.

It has not yet been adequately demonstrated by direct comparison between "old" and "young" hydras that there is no difference between them. In an attempt to throw light on this matter, the budding rates and tentacle numbers of parent hydras and of their youngest buds in a line of successive first buds were compared, both under normal conditions and under radiation stress.

Two groups of 20 *Hydra littoralis* lacking buds and gonads were selected at random from a large male clone and reared by Loomis's culture method (*10*) in individual 10-ml beakers each containing 5 ml of water. One group was irradiated with a dose of 2000 r of x-rays. Detached buds were isolated daily. A dose of 2000 r was chosen because this was the highest dose that did not decrease the budding rate.

The number of buds produced by each 4th-, 8th-, and 12th-generation offspring in each line of successive first buds was compared with the number of buds produced by the corresponding original parent over a 15-day period, and the mean differences were evaluated by Student's t test. Presumably fewer cell divisions occurred in the history of a bud produced by one of the parents than in that of one of the buds derived from a bud, several generations removed, of a parent. Thus, the performances of "old" (the original parents) and of "young" hydras were compared during the same period of time and under the same conditions. The results are summarized in Table 1.

As the original parents in the nonirradiated group became older, their budding rate became progressively slower compared with that of young hydras. At the 12th generation the difference was highly significant ($p < .005$). The irradiated hydras followed this same trend between the 4th and 8th generations ($p < .05$), but in these experiments the results are not conclusive at the 12th generation ($p = .07$). These results seem to support the hypothesis that older hydras bud more slowly than younger ones.

There was no significant difference between the budding rates of irradiated and nonirradiated hydras, compared group by group (Table 2), but there was some indication that doses of from 100 to 2000 r stimulate budding during the first week after irradiation.

The number of tentacles of each hydra in these experiments was recorded daily, and comparisons were made between the mean numbers of tentacles for the various groups. In contrast to the results of Hase and Grosz, no significant differences were found. Also, there was no increase with time in the mean number of tentacles of the original parents. We conclude that the number of tentacles does not increase with age in *Hydra littoralis*.

At the end of the first month of the experiments the hydras suffered from a depression possibly caused by traces of detergent left in the glassware when it was washed. Thirty-two percent of the original parents but only 8 percent of the youngest buds (in generations 2 through 6) became badly depressed. Six days later 7.5 percent of the original parents but only 2.5 percent of the youngest buds had died. This increased susceptibility of older hydras supports the hypothesis that aging takes place (*11*).

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19 April 1961

Radiation Dosimeter Utilizing the Thermoluminescence of Lithium Fluoride

Abstract. A dosimeter, with little wavelength dependence and large useful energy range for electromagnetic radiation, which is simple to use and read, has been developed. It appears to have applications in personnel monitoring as well as radiation research.

A radiation dosimeter has been developed which utilizes the thermoluminescence properties of lithium fluoride crystals. The principles involved in such dosimetry have been previously described by Daniels *et al.* (*1–3*). A CaF_2 : Mn thermoluminescent dosimeter has recently been developed by Schulman *et al.* (*4*).

The phenomenon of thermoluminescence in crystals may be described as "frozen-in" or stored luminescence which is unavailable at normal temperatures but which may be recovered by heating. It is due to the trapping of electrons displaced by high-energy radiation. The amount of thermoluminescence stored in a given crystal is proportional to the amount of previous exposure to ionizing radiation. For dosimetry purposes the thermoluminescence must be stable in the temperature range of normal use, that is, it must have a high activation energy relative to room temperature. Several materials, including CaF_2, LiF, $CaCO_3$ (calcite), and SiO_2, have the capacity for such high-temperature thermoluminescence.

Lithium fluoride has a high-temperature thermoluminescence particularly suited for dosimetry purposes. As a

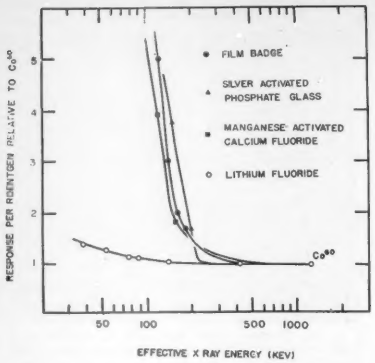

Fig. 1. Energy dependence of LiF compared with that of other dosimeters.

compound, LiF is inert, insoluble, and nontoxic. It has hard crystals which are stable in air and relatively free from mechanically induced luminescence. The thermoluminescence of LiF has an almost linear response to amount of radiation over a range of a few milliroentgens to many kiloroentgens. Because of the low atomic number of both lithium and fluorine, the energy dependence of LiF thermoluminescence is small compared with that of other common dosimeters (see Fig. 1). It is noted that over the range from 40-Kev effective x-rays to the 1.1- and 1.3-Mev gamma rays from cobalt-60, the thermoluminescence varies by only 40 percent. In addition, LiF luminescence systematically responds to alpha, beta, and neutron irradiation (*2*), thus making possible composite measurements of ionizing radiation. The LiF dosimeter shows less than measurable isothermal decay at 50°C for 1 day, and thereby assures a long-range retention of accumulated thermoluminescence.

The dosimeter now in use by this laboratory consists of powdered LiF crystals (*5*). No attempt has been made so far to control the concentration of luminescence activators. However, the efficiency of the dosimeter for low-level radiation will perhaps improve with the use of optimum-activated crystals. The present dosimeter is prepared by grinding and mixing pure, fused LiF in order to average out chemical and physical inhomogeneities. The washed and screened powder (100–200 Tyler) is then annealed to eliminate the undesirable low-temperature thermoluminescence previously described (*3*). Consequently, annealed LiF powder is used in the present dosimeter, either free or in containers. Tubes and capsules of gelatin, vinyl, and polyethylene have been used to date; no special shielding is necessary to improve the energy dependence.

To measure the thermoluminescence quantitatively after irradiation, a measured volume of powder is placed under a photomultiplier tube and heated to a temperature of about 250°C in a period of less than 1 min. The thermoluminescence intensity is integrated by collecting the photomultiplier current on a Mylar capacitor and then measuring the voltage of this capacitor with an electrometer voltmeter. By the use of this technique the thermoluminescence of a given sample may be reproduced with a standard deviation of 2 percent.

An example of this dosimeter in medical use is illustrated in Fig. 2. The catheter containing a long plastic tube of powdered LiF is placed in the rectum of a patient who is receiving internal radiation treatment. Figure 2 shows a touched up x-ray of a radioactive applicator in place, with the values of the radiation dose in rads after 24 hr listed adjacent to the dosimeter tube. Dose measurements in vivo during such treatment are useful to prevent excessive radiation to the rectum and to determine the length of the treatment. Figure 3 shows a similar laboratory test under controlled conditions with a radium standard used as a source of radiation. The solid line represents the calculated theoretical dose and the dots represent the measured values.

With a sensitized LiF dosimeter it might be possible to have any member of the population carry a dosimeter attached to his person. Accurate measurements of radiation doses to members of the general population would then be available in case of an atomic attack. Dosimetry information would also be of interest in measuring average radiation to the general population under peacetime conditions. The LiF dosimeter would also be useful to persons who have some contact with radiation in their daily work but not sufficient exposure to warrant the usual monitoring methods now available. The accumulated dose on these monitors could then be read yearly or whenever a person changes employment.

Such a dosimeter could also play an important role in research. The cost of the dosimeter is small enough to warrant the monitoring of individual animals undergoing radiation experiments (*6*).

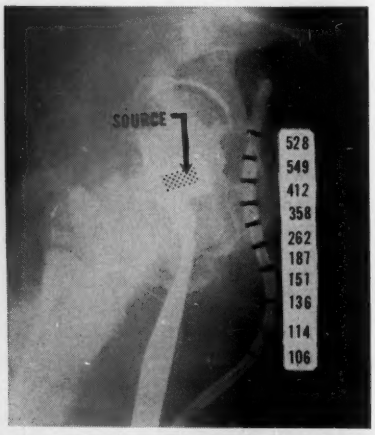

Fig. 2. Touched up x-ray, showing dosimeter tube in rectum near the radioactive source. Values are 24-hr dose in rads.

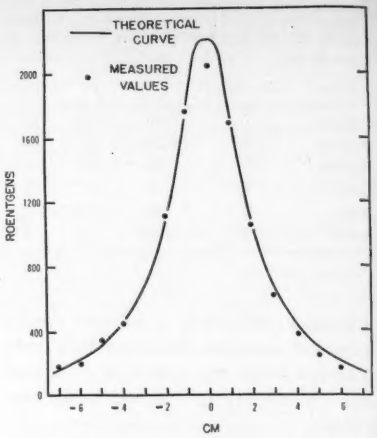

Fig. 3. Comparison of theoretical and measured values obtained by using the dosimeter tube near a radium source.

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6. We are pleased to acknowledge support for part of the work by the U.S. Atomic Energy Commission and the Wisconsin Alumni Research Foundation. The earlier work was supported by the Army Chemical Corps.

27 March 1961

Protection of Mice against Lethal Staphylococcus Infection by Escherichia coli O_{86} Fractions

Abstract. Small doses of protein-lipopolysaccharides and lipopolysaccharides from *Escherichia coli* O_{86} prevent the death of mice infected intraperitoneally with a clinically virulent *Staphylococcus aureus.*

The increasing seriousness of antibiotic-resistant staphylococcal infections in man and the established effectiveness of some polysaccharides in the prevention of experimental infections due to Gram-negative bacteria prompted the present investigation. Landy (*1*) found that lipopolysaccharides from Gram-negative bacteria were quite ineffective against infection of mice with even minimal amounts of *Staphylococcus aureus*. Dubos and Schaedler (*2*) noted that mice became either more resistant or more susceptible to subsequent intravenous infection with virulent staphylococci, depending on the amount and the time interval between treatment with either Pertussis or Klebsiella vaccine, both of which contain endotoxin. Under optimal conditions, the authors noted a marked increase of resistance to staphylococcal infections. Nevertheless, the death rate of mice was still between 40 and 100 percent 12 to 15 days after the challenge. More recently these investigators reported considerable enhancement of mortality due to staphylococcal infection in mice, if minute amounts of endotoxin were given simultaneously with a challenge dose of staphylococci (*3*).

In the present experiments, litter mates of Swiss albino mice (Huntingdon Farms, Inc.), predominantly male, 5 to 6 wk old and weighing 18 to 25 g, were used. The animals were given free access to Purina Chow and water. For protection the mice were injected intraperitoneally with a solution in 0.25 ml of 0.85 percent saline of (i) protein-lipopolysaccharides or (ii) lipopolysaccharides, the purest of which contained <1 percent nucleic acids [analytical data: (i) C, 51.6; H, 8.3; N, 4.7; P, 2.6; and (ii) C, 45.5; H, 6.9; N, 1.9; P, 1.96] from blood group B active *E. coli* O_{86} (*4*), prepared by established procedures (*5*). Since both the protein-lipopolysaccharides and lipopolysaccharides showed approximately the same biological activities, no differentiation is made.

The LD_{50} of this material, given intraperitoneally, was approximately 700 μg per mouse. Control animals received intraperitoneally 0.25 ml of physiological saline.

The animals were challenged intraperitoneally with the coagulase positive *Staphylococcus aureus* phage type 44A (*6*). A dose of 1.1 to 1.3 $\times$ 10^8 cocci, causing death in 85 to 100 percent of the mice within 6 to 24 hr, was administered in 0.25 ml of physiological saline. Mice are much more resistant to intravenous inoculation with this organism than to intraperitoneal injection (*6*) where the LD_{50} was 1.5 to 2.5 $\times$ 10^7 microorganisms.

Staphylococci were grown and the concentration adjusted according to the method of Higginbotham and Dougherty (*6*), except that the concentration of bacteria was initially adjusted to a standard turbidity in the Klett-Summerson colorimeter with a red No. 66 filter.

Survival of the mice was determined 16 to 36 days after application of the challenging dose of staphylococci. The similar results of 14 experiments, in which the interval between the second lipopolysaccharide treatment and challenge was 16 to 72 hr, are summarized in Table 1. Ten micrograms injected twice intraperitoneally in an interval of 24 hr prevented death due to staphylococcal challenge in 106 out of 110 mice. A similar but weaker effect was obtained when two times 100 μg of the polysaccharide material was injected subcutaneously with the challenge still being carried out intraperitoneally.

Table 2 shows the time dependence of the effect of the *E. coli* O_{86} polysaccharides between one administration of polysaccharide and challenge by staphylococci. The polysaccharide fractions gave full protection if inoculated intraperitoneally 16 to 48 hr before and over 50 percent protection when given 6 to 12 hr prior to challenge. A single injection of *E. coli* O_{86} fractions more than 75 hr or less than 5 hr prior to or shortly after administration of staphylococci, gave little or no protection. The application of *E. coli* O_{86} polysaccharide complex subcutaneously also afforded protection if the interval between injection of protective material and challenge was more than 10 hr. Numerous other polysaccharides such as blood group active preparations from *Sassafras, Taxus,* and erythrocytes (*7*), as well as the monosaccharides 2-O-methyl-L-fucose, 2-O-methyl-D-fucose (*8*), and two crystallized brain gangliosides, showed no effect at similar concentrations. In addition, force feeding of the test animals with three times 200 mg each of *E. coli* O_{86} polysaccharide over a 3-day period with the last feeding 20 hr prior to challenge did not lower the death rate.

These results have been uniformly reproducible over a period exceeding 1 yr. They are noteworthy in that they point to the possibility of approaching the therapy of staphylococcal infections by other than classical methods. The protective action of the polysaccharide material and the peculiar time interval essential for its effectiveness merit further investigation. It is to be noted, however, in interpreting these findings, that protection by these preparations has been tested against only one virulent strain at concentrations which, while approximately 100 percent lethal, exceed the LD_{50} only by about one decadic logarithm. Furthermore, the induced lethal staphylococcal infections in mice used in these experiments are hardly comparable to human staphylococcal infections (*9*).

Note added in proof: Similar results have now been obtained with *E. coli* O_{128} lipopolysaccharide prepared in this laboratory.

Table 1. Protection of mice by *E. coli* O_{86} (protein-) lipopolysaccharide complexes against lethal *Staphylococcus aureus* infection 16 to 72 hr later. Route: i.p., intraperitoneal; s.c., subcutaneous.

Polysaccharide complex administration		Deaths	
Amt.* (μg)	Route	No. after 20 to 30 days	Percentage
20	i.p.	4/110	3.6
2	i.p.	9/40	23
200	s.c.	15/50	30
20	s.c.	21/30	70
None		116/130	89

* Divided into two equal lots and given 24 hr apart.

Table 2. Influence on protection of time interval between injection of polysaccharide complex and challenge.

Interval before challenge (hr)	Deaths	
	No. after 16 days	Percentage
10 μg intraperitoneally		
2 to 4	32/50	64
5 to 6	10/20	50
8 to 9	2/20	10
11 to 12	2/20	10
16 to 48	0/50	0
No polysaccharide complex	49/55	89

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9. This research was supported by the National Institutes of Health grant No. A-2671 and the National Science Foundation grant No. G-10906. We are grateful to R. D. Higginbotham for a culture of his staphylococcus strain and to Richard Kuhn for the crystallized brain gangliosides.

* Established investigator of the American Heart Association.

30 March 1961

Axenic Cultivation of Entamoeba histolytica

Abstract. *Entamoeba histolytica* (National Institutes of Health strain 200) has been maintained in axenic culture through 50 transfers over a period of 6 months. The medium used is diphasic and contains a cell-free extract of chick embryo which is essential for growth. Inocula of 50,000 amoebas yield 150,000 to 200,000 organisms in 72 hours of incubation at 35°C. An extract prepared from boiled embryos supports growth equally well.

Cultures of *Entamoeba histolytica* are readily established in association with certain species of bacteria or trypanosomatids. In the absence of these microbial associates, cultures are difficult to initiate and thus far have been established only in the presence of intact metazoan cells, namely, chick embryo cells (*1*, *2*). To my knowledge there is no published report presenting unequivocal evidence of the axenic cultivation of this amoeba—that is, the indefinite subcultivation of amoebas in an environment free of metabolizing bacteria, fungi, protozoa, or metazoan cells. Evidence that axenic cultivation of a strain of *E. histolytica* has been achieved is presented in the present report.

The medium used is diphasic. The ingredients of the nutrient broth employed in both phases are listed in Table 1. To prepare the base, 1.6 g of agar are added to 80 ml of nutrient broth and the mixture is boiled, distributed in 4-ml portions to screw-capped tubes (16 by 125 mm), autoclaved for 10 min (15 lb, 121°C); cooled, and stored in the refrigerator. One week before use the base is melted, 1 ml of horse serum (inactivated 30 min, 56°C) is added per tube, and a slant with a short butt is made. After the slant hardens it is overlaid with 3.25 ml of sterile diluted nutrient broth (1:4, with distilled water) containing 0.05 percent agar and is then replaced in the refrigerator for 1 wk. Immediately before use the medium is brought to room temperature, and to the overlay are added 1.5 ml of chick embryo extract and 0.25 ml of vitamin supplement No. 109 (*3*).

Table 1. Ingredients of nutrient broth used in preparation of the diphasic medium for axenic cultivation of *Entamoeba histolytica* [*p*H adjusted to 7.2 with 1*N* NaOH; autoclaved for 10 min (15 lb, 121°C)].

Ingredient	Amount
Tryptose (Difco)	1.00 g
Trypticase (BBL)	1.00 g
Yeast extract (BBL)	1.00 g
Glucose	0.50 g
L-Cysteine hydrochloride	.10 g
Ascorbic acid	.02 g
NaCl	.50 g
KH_2PO_4	.08 g
K_2HPO_4 (anhydrous)	.08 g
Water (distilled)	80.00 ml*
Resazurin (0.05–percent aqueous solution)	0.02 ml

* Or as much as is needed.

Extracts are prepared from 11- or 12-day chick embryos. These are harvested aseptically and, after removal of the eyes and beak, are cut into two or three pieces, weighed, and processed in one of two ways. In one process the extract is prepared by a modification of the "mild extraction" technique (*4*). Embryos are quick-frozen in a Dry Ice–alcohol bath and placed in the refrigerator, and 1 hr later 3 ml of autoclaved, chilled, buffered saline (NaCl, 5.0 g; KH_2PO_4, 1.6 g; Na_2HPO_4, anhydrous, 1.6 g; distilled water, 1000 ml or as much as needed, *p*H 6.8) are added per gram of tissue. Extraction is carried out for 96 hr at 3°C. The extract is then strained through sterile cheesecloth and centrifuged for 30 min (1000*g*, 0°C). The supernatant fluid is collected aseptically, distributed in 10-ml portions to screw-capped tubes, quick-frozen in Dry Ice and alcohol, and stored at −22°C. This material, 25-percent, mild, chick embryo extract, is referred to hereafter as $CEEM_{25}$.

In the other process, boiling buffered saline is poured over the embryos (3 ml/g). The embryos are then boiled for 2 min, cooled to room temperature, and refrigerated (3°C) for 24 hr. Further processing is similar to that described for the preparation of $CEEM_{25}$. The second extract, 25-percent, heated, chick embryo extract, is hereafter referred to as $CEEH_{25}$. Each batch of extract is checked for microbial contaminants by the procedure which is outlined below.

For detection of bacterial and fungal contaminants of extracts and cultures, the following media are used: fluid thioglycollate, brain-heart infusion with 0.1 percent agar, Sabouraud's broth, trypticase soy agar plates with 5 percent sheep blood, and PPLO (*5*) agar plates (Difco) with 20 percent human blood. The fluid media, in 50-ml quantities, are inoculated with 0.25-ml samples, the plates with 0.05-ml samples. Fluid thioglycollate and brain-heart infusion are incubated at 25°, 35°, and 55°C; Sabouraud's broth and agar plates are incubated at 25° and 35°C. All are kept under observation for 7 days. In testing cultures containing antibiotics, 1-ml samples are transferred from the first set of liquid test media to a second set and also incubated for 1 wk. To detect trypanosomatids, tubes of STB medium (*6*) are inoculated with 0.25-ml samples, incubated at room temperature, and observed for 14 days.

Amoebas (NIH strain 200) grown in association with a trypanosomatid of the genus *Crithidia* (*7*) were used to initiate axenic cultures in medium containing $CEEM_{25}$. The monoxenic source cultures were started with amoebic cysts isolated with a micromanipulator after a wash in dilute HCl. Two sets of axenic cultures (I and II) were established, the first with inocula of 500,000 amoebas, the second with 150,000. Incubation was carried out at 35°C. First transfers were made after 24 or 48 hr, second and third at intervals of 48 or 72 hr. At this point multiplication of the amoebas slowed, and it was necessary to extend the time between transfers to 5 and even 7 days. After the seventh transfer, cultures showed renewed vigor, and thereafter transfers were made alternately at 72 and 96 hr. In well-established cultures, inocula of 50,000 amoebas yielded 150,000 to 200,000 organisms in 72 hr. Subcultures were made by removing the relatively amoeba-free upper half of overlay and transferring 0.5 to 1.5 ml of the remainder to fresh medium.

Set I cultures were initiated in the presence of penicillin G and dihydrostreptomycin sulfate (250 units and 0.25 mg, respectively, per milliliter of over-

lay). This set has undergone 50 transfers during a 6-mo period. After the 16th transfer a subline was started in antibiotic-free medium. It has undergone 34 transfers. No antibiotics were employed in set II cultures; this was to rule out possible effects of these agents in preventing detection of certain bacterial contaminants. Set II cultures were discontinued after the 15th transfer, when tests showed clearly that axenic cultivation had again been achieved.

Repeated sterility checks failed to uncover any evidence of cryptic microbial contamination of the amoebic cultures. Gross contamination occurred in approximately 2 percent of some 800 tubes used and was traceable in each instance to airborne contamination which occurred during subculturing. Tests with STB medium demonstrated that *Crithidia* introduced with the original inoculum of amoebas died out prior to the third transfer.

The effect of heat on growth-promoting factors present in embryo extract was investigated. A subline from set I cultures was started in medium containing $CEEH_{55}$. Yields from this subline (still in existence after 29 transfers) were equal to those obtained with unheated extract. These results were unexpected in light of earlier studies (*2*, *8*) which showed that even milder heat treatment destroyed growth-promoting activity. The highly supplemented nature of the diphasic medium may explain, in part, the results obtained. Baernstein *et al.* (*8*), in working with amoebas grown in microcultures, discovered that enriching their medium with vitamins, amino acids, and ribonucleic acid partially restored factors that had been lost through heating the extracts (*9*).

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20 April 1961

Intracellular Study of Recurrent Facilitation

Abstract. Recurrent facilitation in the cat's spinal cord has been studied in deep peroneal and quadriceps motoneurons with the use of intracellular recording. The presence of facilitation was indicated by several criteria, among them increased firing index of the cells or decreased latency of firing. In many, but not all, facilitated cells the conditioning volley caused a small visible depolarization. Subthreshold synaptic potentials were frequently increased in magnitude by the conditioning volley, which also increased the effectiveness of a stimulus applied through the microelectrode. Facilitation was found in a large percentage of the motoneurons investigated and was clearly able to bring about pronounced changes in the excitability and firing behavior of these cells.

Previous experiments in this laboratory have shown that recurrent inhibition and recurrent facilitation are distributed in an organized manner in the cat spinal cord (*1*), and subsequent work has suggested that the facilitation may in fact be a disinhibition which enhances reflex discharge by decreasing background inhibitory activity (*2*). The purpose of the present investigation has been to record, in individual motoneurons, the intracellular changes which accompany recurrent facilitation of reflex discharge, in order to study the distribution of this phenomenon among motoneurons and to obtain further evidence on the synaptic mechanism of recurrent facilitation.

All experiments have been performed on cats whose spinal cords had been severed in the upper cervical region, and the preparation was the same as previously described (*1*, *3*). So far, studies have been made of motoneurons of the deep peroneal group and of quadriceps whose action is usually facilitated by antidromic stimulation of the nerve to gastrocnemius-soleus and biceps-semitendinosus respectively (*1*). Intracellular recording was by means of glass micropipettes with tip diameters less than 1 μ, filled with 2.7*M* KCl.

The cells that have been studied had action potentials ranging from 50 to 100 mv. Synaptic activity was frequently visible in the absence of electric stimulation and occasional firing was observed in several cells as a result of such activity. Many deep peroneal cells fired repetitively to single dorsal root shocks, in a manner similar to that described for cells whose activity was recorded in ventral root filaments (*4*); it was often possible to obtain as many as four to five responses, the intervals between spikes being as short as 2.5 msec. Such repetitive discharges were superimposed on long and complex synaptic potentials. Many of the penetrated cells had a monosynaptic firing index (*5*) of 100. Such cells were studied either by weakening the strength of the dorsal root volley or by restricting stimulation to a small dorsal rootlet. In this manner it was possible to make a cell respond either with an intermediate monosynaptic firing index or polysynaptically.

Facilitation of single motoneurons was studied only in preparations in which visible recurrent facilitation of the monosynaptic reflex was present. Upon penetration it was first essential to determine whether the cell was facilitated. This was done employing a number of criteria: in many cases a conditioning shock increased the firing index; at times the latency of a polysynaptic discharge was reduced; conditioning has also been seen to increase the number of spikes in the discharge.

Facilitation has been studied in 103 cells, and changes in membrane potential were looked for in a number of these. In many cases the conditioning shock caused small depolarizations, the largest being less than 3 mv. In other facilitated cells depolarizations were much smaller and in some cases they were either absent or vanishingly small. The depolarization shown in Fig. 1 is typical. While it is hard to determine its exact onset, it first becomes clearly evident about 6 msec after the conditioning stimulus and has a time course of approximately 50 msec. These values are compatible with the latency and duration of recurrent facilitation as exemplified in typical facilitation curves (*3*).

As a result of a conditioning volley, subthreshold synaptic potentials in facilitated cells were frequently measurably increased over a considerable part of

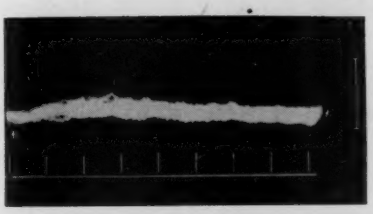

Fig. 1. Depolarization evoked in a deep peroneal motoneuron by an antidromic volley in the nerve to gastrocnemius-soleus. Conditioning stimulus delivered at the arrow. This record was obtained by superimposing approximately 15 faint traces. Time, 10 msec, voltage calibration, 10 mv

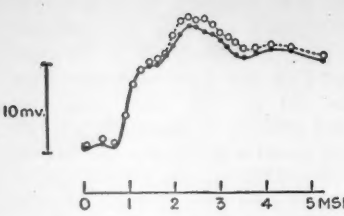

Fig. 2. Effect of conditioning volley in nerve to gastrocnemius-soleus on subthreshold excitatory postsynaptic potential evoked in a deep peroneal motoneuron by stimulation of L6 DR and the upper half of L7 DR. Conditioning-test interval, 20 msec.

their time course. Such an increase in excitatory postsynaptic potential (EPSP) is shown in Fig. 2. The deep peroneal motoneuron concerned initially had a monosynaptic firing index of 0, and a polysynaptic firing index of 100. The firing index of the polysynaptic response, which latter, judging by its latency, was disynaptic, could be modified by recurrent facilitation; at two different levels of orthodromic drive it was increased from 0 to 26 and from 33 to 90. In order to measure the effect of recurrent conditioning on the EPSP, groups of control and conditioned responses were alternated and photographed on moving film. Changes in the subthreshold EPSP were then determined by measuring the amplitude of these conditioned and unconditioned EPSP's at each of 23 different intervals following the stimulus artifact. The second beam of the oscilloscope was used as an arbitrary reference for measurement of EPSP amplitude. The solid line (dots) in Fig. 2 represents the average control EPSP; the dashed line (circles), the average conditioned EPSP. Tracings of conditioned and unconditioned membrane potentials revealed little or no shift in resting potential as a result of conditioning. There was also no difference between the early parts of the two groups of EPSP's. However, most of the later part of the potential was significantly increased by recurrent conditioning ($P < 0.02$). Changes of this type have been seen in a number of motoneurons, and increases in EPSP's have generally been more marked in the later part of the potential.

Intracellular stimulation of motoneurons by means of a bridge circuit similar to that used by Frank and Fuortes (*6*) has shown that an intracellular stimulus delivered through the micropipette is generally made more effective by recurrent conditioning. In the case of the cell whose EPSP is illustrated in Fig. 2, at three different strengths of intracellular stimulation, namely wth current pulses 7.5 msec in duration and ranging from 2.25 to 2.5 $\times 10^{-8}$ A, conditioning increased the firing index from 0 to 19, from 8 to 32, and from 28 to 69. This increase in intracellular firing index is of the same order of magnitude as that of the disynaptic firing index described above.

These observations made by means of intracellular recording are consistent with the hypothesis that recurrent facilitation is due to a reduction of background inhibition. Reduction of tonic inhibitory action and the consequent slight decrease in membrane conductance could lead to both the effects on membrane potential and changes in excitability which have been seen. However, other interpretations of the findings available so far may also be possible and further experiments designed to clarify the meaning of the membrane changes are under way at this time.

Facilitation has been looked for so far in 93 deep peroneal cells and 10 quadriceps motoneurons, and has been found, as evidenced by the criteria listed above, in 59 of the former and 8 of the latter. Eccles, Iggo and Ito (*7*) have found that in cats lightly anesthetized with sodium pentobarbitol, and with the spinal cord sectioned at L2, recurrent facilitation, as judged by the presence of a small depolarization, is recorded very infrequently. And Granit and Rutledge (*8*) have interpreted the findings of these workers as showing that "recurrent facilitating effects were rare and very small." As shown above, the changes in membrane potential that accompany recurrent facilitation are indeed small. However, the fact that facilitation has been found in 63 percent of the deep peroneal neurons and in most of the quadriceps cells that have been studied shows that in the unanesthetized high spinal cat this phenomenon is certainly not rare. Furthermore, while the membrane changes recorded have been small, pronounced changes in firing index have been seen in a number of cells. Clearly, recurrent facilitation is a widespread phenomenon in certain motoneuron nuclei and appears capable of bringing about significant changes in motoneuron firing (*9*).

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20 April 1961

Recovery of the Living Fossil Mollusk, Neopilina, from the Slope of the Cedros Trench, Mexico

Fourteen small monoplacophoran mollusks, relict animals with a discontinuous geologic range between the Paleozoic and the Recent, have been recovered from a biological trawl sample taken 31 December 1960 from the slope of the Cedros Trench, Baja California, Mexico (*1*). Specimens of *Neopilina* previously have been reported from off Costa Rica, off Peru, and off Cape San Lucas, Mexico (*2*). This collection represents the most northern record for the Monoplacophora as well as the largest single collection.

The specimens (Fig. 1) are from the Allan Hancock Foundation station No. 7230–60, located 30 mi off Natividad light, Baja California, Mexico, between 27°52′25″ to 27°51′30″N and 115°44′30″ to 115°45′15″W (dead-reckoning position). The depth varies between 1514 fathoms at the start of the station to 1493 at its completion. The specimens range in size between 1.3 mm and 2.37 mm long.

The minute animals collected have six pairs of diminutive gills and a segmental musculature similar to that described by Lemche and Wingstrand (*3*)

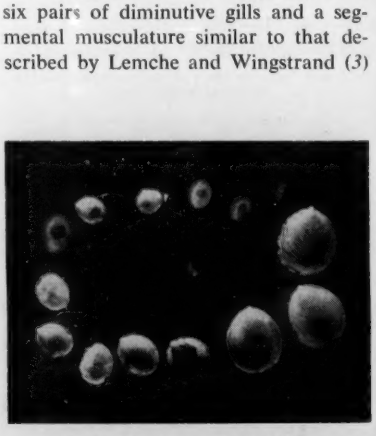

Fig. 1. Specimens of Neopilina.

for *Neopilina* (*N.*) *galatheae* Lemche. The six pairs of gills suggest that the animals belong to *Neopilina* (*Vema*) rather than to *Neopilina* (*Neopilina*), but the exact assignment of the specimens to one of the two known species remains uncertain. This uncertainty is due to the fact that the specimens are apparently different in shell sculpture from both *Neopilina* (*Neopilina*) *galatheae* Lemche and *Neopilina* (*Vema*) *ewingi* Clarke and Menzies (*4*).

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References and Notes

1. The net of the biological trawl was nylon with a mesh diameter of 0.5 mm. The position and correction of sonic fathoms was provided by Elizar Uchupi. The cruise was supported by National Science Foundation grant No. 12329 to K. O. Emery of the Geology Department of the University of Southern California.
2. Data regarding the positions of other captures of *Neopilina* are given in a paper by Menzies *et al.* [*Oikos* **10**, 168-182 (1959)]. We understand that a description of the capture of *Neopilina* by the Scripps Institution of Oceanography from the slope off Cape San Lucas, Mexico, is scheduled for publication (information courtesy of Robert Parker, Scripps Institution of Oceanography, La Jolla, Calif.).
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4. A detailed study of the shell sculpture is in progress. A report is in preparation on the ecological conditions and the fauna associated with the monoplacophorans with the hope that such information will aid our understanding of the ecology of these unusual animals and with the hope that the data will assist in their future capture.

20 April 1961

Molecular Weight Determinations

Abstract. A Beams magnetically suspended equilibrium ultracentrifuge was used to determine the molecular weight of sucrose, ribonuclease, and insulin. Both long- and short-column ultracentifuge cells were used. The longer cells gave greater precision, but required a longer time for equilibrium to occur.

The Beams type magnetically supported equilibrium ultracentrifuge (*1*) has been used to determine the molecular weights of a number of substances, including sucrose, ribonuclease, and insulin. The measurements were made to test the reliability of the apparatus as well as to determine directly the molecular weight values.

For a monodisperse substance in a dilute solution, the molecular weight (M) is given by the relation (*2*):

$$M = \frac{2RT \ln \frac{f_2 c_2}{f_1 c_1}}{(1 - Vd)\ 4\pi^2 N^2\ (r_2^2 - r_1^2)}$$

where N is the rotor speed in revolutions per second, T is the temperature, c_1 and c_2 are the concentrations at the radial distances r_1 and r_2, respectively, f_1 and f_2 are the activity coefficients, and V is the partial specific volume. The rotor speed is determined with a precision of 1 part in 10^5, the temperature is measured to at least 1 part in 10^4, and the ratio c_1/c_2 is determined to 1 part in 10^3. The quantities $(1 - Vd)$ and the activity coefficients are measured outside the centrifuge and are the least precisely known of the factors in the equation.

The sucrose was obtained from National Bureau of Standards lot No. 5706 with the solvent triply distilled water. The concentration was determined with a microbalance. The specific refractive increment was measured in this laboratory and is in agreement with the value obtained by interference methods. Chromatographically pure crystalline bovine ribonuclease was obtained from the Sigma Chemical Company. The solvent used was a solution of 0.1M NaCl, 0.035M K_2HPO_4, and 0.004M KH_2PO_4, having a pH of 7.7. A quantity of crystalline zinc-insulin was kindly furnished by Merck, Sharp and Dohme Research Laboratories. The solvent was 0.1M KH_2PO_4 and 0.0033M H_3PO_4 with a pH of 2.8.

Typical results obtained are listed in Table 1. It should be noted that greater accuracy is obtained with the longer cells, but more time is required to reach equilibrium. Consequently, short cells should be used if denaturation occurs during a relatively long experiment (*3*).

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2. T. Svedberg and K. O. Pedersen, *The Ultracentrifuge* (Oxford Univ. Press, London, 1940).
3. We should like to thank J. W. Beams for his help and invaluable advice on this project. The work was supported by a grant from the National Institutes of Health.

10 March 1961

Table 1. Typical results of molecular weight determinations. M_o is the formula weight; M_{obs}, observed molecular weight; t, time required for the experiment, in hours; L, length of the ultracentrifuge cell, in millimeters; c, concentration, in g/100 ml; and N, frequency of the rotor, in rev/sec.

t	L	c	N	M_o	M_{obs}	$(1 - Vd)$
			Sucrose			
22	8	2.990	398.95	342.3	341.9 ± 0.58	0.3761
4	3	2.988	262.10	342.3	343.5 ± 1.40	.3762
			Ribonuclease			
62	8	0.281	174.00	13,663	13,650 ± 23	.3016
14	3	.241	235.96	13,663	13,696 ± 58	.3016
			Insulin			
35	5	.152	306.02		11,427 ± 31	.2606
12	3	.365	267.44		11,517 ± 46	.2606

Constitution and Smoking

Abstract. Among 167 adult male factory workers of Neapolitan parentage but of American birth or upbringing, the lean men smoked significantly more than the fat ones. Smoking was positively correlated with serum cholesterol but was not associated with morphological masculinity, blood pressure, diet, or consumption of alcohol.

The detection of determinants of tobacco smoking would help in understanding and possibly preventing diseases associated with smoking, notably lung cancer, emphysema, chronic bronchitis, and cardiovascular disease. The search for constitutional correlates of smoking is being conducted chiefly along psychological lines (*1*). A few investigators (*2–4*) have reported associations of smoking habits with physique and blood pressure, but at borderline levels of significance or with inconsistent direction.

Since the use of tobacco may vary from one cultural group to another, it is desirable to study subjects with a common culture. If, in addition, the subjects have similar biological backgrounds and thus constitute a relatively homogeneous group, any associations found between smoking and other personal characteristics take on added meaning.

Such a group has been under investigation since 1956 (*5*). In 1958 it comprised 167 male factory workers whose parents were born within 75 miles of Naples, Italy; of the men themselves, 151 were born and raised near Boston, Mass., and the other 16 near Naples. Seven of the Italian-born men had been brought to the United States before the age of 10, and nine men had come to this country when they were 10 or older. Of 300 males employed in a single factory (*6*) who met the criteria of age (20 to 59 yr),

Table 1. Associations of smoking with physique and serum cholesterol among 167 Italian-American factory workers.

Characteristic	*P* value (χ^2)	Biserial coefficient of correlation	
		Non-smokers versus smokers*	Non-smokers and light smokers versus heavy smokers†
Bi-iliac breadth	.10	−.05	−.23
Serum cholesterol	.10	.32	.23
Bi-iliac breadth/biachromial breadth	.05	.04	−.26
Subscapular skinfold	.05	−.19	−.16
Ectomorphy	.05	.25	.29
Weight	.01	−.25	−.37
Height/(cube root of weight)	.01	.25	.29
Endomorphy	.01	−.21	−.28

* Standard errors for all values in column 3, ± 0.11.
† Standard errors for all values in column 4, ± 0.09–0.10.

Neapolitan parentage, and American birth or upbringing, 213 had volunteered for a long-range study of coronary heart disease. Thirteen were eliminated from the study in 1956 for various technical reasons. Thirty-three more dropped out between 1956 and 1958: 17 declined to participate further, 13 were no longer employed by the firm, 2 were ill, and 1 had died. While nothing is known about those who did not volunteer initially, it is known that the 33 men dropped between 1956 and 1958 did not differ in smoking habits ($p < .70$) from the 167 who remained in the study: 11 men aged 20 to 29 yr, 63 aged 30 to 39, 77 aged 40 to 49, and 16 aged 50 to 59.

Smoking was graded in five categories: 0, if the subject was not currently smoking and had never been a regular smoker; 1, rare or occasional smoking (for example, one to two cigars or pipes a day or one to five cigarettes a week, but no combination of these) 2, regular smoking, less than 20 cigarettes or five cigars or pipes a day; 3, 20 to 30 cigarettes or 6 to 10 cigars or pipes a day; and 4, more than this. The 12 men who had stopped smoking were arbitrarily placed in grade 2. There were 30 nonsmokers (18 percent); of the 137 smokers, 8 smoked cigars only, 3 smoked pipes only, 1 smoked cigars and pipes, 1 smoked cigars and cigarettes, and 124 smoked cigarettes only. Grade 1 contained 9 men; grade 2, 35; grade 3, 78; and grade 4, 15.

Standard techniques were followed for anthropometry (*7*), for somatotyping (*8*), and for serum cholesterol (*9*) and blood pressure determinations. Dietary data were obtained through a 45-minute interview, a modified Burke diet history (*10*), and a detailed questionnaire filled out by whoever prepared the subject's food at home. Activity was graded, by a physician, in five categories based on estimated exertion both on and off the job. The anthropometric observations included data of several kinds descriptive of body form.

1) Standard dimensions [height, weight, and biacromial (shoulder) and bi-iliac (hip) breadths] and certain ratios derived from them (height/cube root of weight), biacromial breadth/height, bi-iliac breadth/height, and biacromial plus bi-iliac breadth/height], reflecting leanness-stockiness and linearity-laterality of build.

2) Data on the thickness of skinfolds in the arm (triceps) and back (scapular) areas, which measure subcutaneous fat.

3) Data on somatotype, comprising photographically based ratings of endomorphy (fat), mesomorphy (bone and muscle), and ectomorphy (linearity); dysplasia (a measure of lack of correspondence among five body regions in respect to the three foregoing somatotype components); and gynandromorphy (a rating of morphological masculinity). Another index developed in an attempt to grade morphological masculinity is Tanner's "index of androgyny" (*11*) (3 times the biacromial breadth minus the bi-iliac breadth).

By the chi-square test, the following factors showed no significant association with smoking ($p > .10$): birthplace; age; height; biacromial breadth; biacromial breadth/height; bi-iliac breadth/height; biacromial plus bi-iliac breadth/height; 3 times the biacromial breadth minus the bi-iliac breadth; triceps skinfold; triceps plus subscapular skinfolds; mesomorphy; gynandromorphy; dysplasia; systolic and diastolic blood pressure; daily caloric intake; and percentages of daily calories contributed by total fat, saturated fatty acids, polyunsaturated fatty acids, protein, carbohydrate, and alcohol. Smoking was associated at the 10-percent probability level with bi-iliac breadth and serum cholesterol; at the 5-percent level, with bi-iliac breadth/biacromial breadth, subscapular skinfold, ectomorphy, and physical activity; and at the 1-percent level with weight, height/(cube root of weight), endomorphy, and somatotype group.

The direction and strength of the associations below the 10-percent probability level were determined by computing biserial coefficients of correlation (*12*), except for somatotype group and activity, which are not amenable to such statistical treatment. Somatotype group consists of 13 combinations of somatotypes grouped by component dominance, primary and secondary. As for activity, inspection of the contingency table showed no regression of activity on smoking—that is, smokers of all grades had very similar activity levels. On the other hand, the most active and the least active men smoked more than those of average activity—a finding which reflects a curvilinear regression of smoking on activity.

For characteristics associated with smoking at or below the 10-percent probability level, Table 1 presents biserial coefficients of correlation computed in two ways: (i) by comparing nonsmokers with all smokers, and (ii) by comparing nonsmokers plus light smokers (grades 0, 1, and 2) with heavier smokers (grades 3 and 4). The latter comparison afforded generally higher coefficients.

The results show a consistent and statistically significant tendency—though not a particularly close one, certainly not close enough to serve as a basis of prediction for individuals—for lean men to smoke more than stout or fat (but not muscular) men. This association, disclosed by all three anthropometric techniques, was not the result of different diets, insofar as can be judged from the dietary constituents considered here, since smoking and caloric intake—total caloric intake as well as intake of component foods—were independent of each other. Absence of the commonly observed increase in smoking with age probably reflects the concentration of ages in the 30's and 40's. The present findings confirm previous reports (*2, 4, 13*) of slightly higher serum cholesterol among smokers; the 30 nonsmokers had a cholesterol level of 212 ± 8.8 mg. (S.E.) per 100 ml of serum; the 137 smokers, a level of 237 ± 3.7 mg (S.E.) ($p < 0.01$). Contrary to findings previously reported, smokers in this series were no less masculine in physique (*3*), were no more active (*4, 14*) and consumed no more alcohol (*14*) than nonsmokers (*15*).

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10 April 1961

Fluorine Substitution Affects Decarboxylation of 2,4-Dichlorophenoxyacetic Acid in Apple

Abstract. Marked differences exist in the rate at which 2,4-dichlorophenoxyacetic acid (2,4-D) is broken down by different plant species and varieties. This activity has been measured by collecting carbon dioxide from leaves treated with carboxyl-C^{14} labeled compounds. The substitution of fluorine for chlorine in the 4-position of 2,4-D inhibits this decarboxylation in leaves which are able to break down 2,4-D rapidly.

It has been reported by Luckwill and Loyd-Jones (*1*) and Edgerton (*2*) that 2,4-dichlorophenoxyacetic acid (2,4-D) is decarboxylated in the leaves of several varieties of apple. The rate of breakdown or decarboxylation was found to be different in several varieties and would appear to be the basis for the resistance of some varieties to the regulatory effects of this compound on growth. With the McIntosh variety, on which sprays of 2,4-D are ineffective in delaying fruit and leaf petiole abscission, the compound is rapidly decarboxylated in the leaf. In Stayman and Winesap varieties, which show a pronounced response to 2,4-D sprays, decarboxylation occurs at a much slower rate (*2*).

In some studies on petiole abscission and fruit drop in 1959 with several growth regulators, it was found that 2-chloro,4-fluorophenoxyacetic acid (2,4-F) had a marked effect on preventing abscission in McIntosh as well as in several other varieties. The formative effects of 2,4-F on shoot and leaf growth of McIntosh were similar to those produced by 2,4-D on a susceptible variety such as Stayman (Fig. 1). Thus the substitution of fluorine for chlorine in the 4-position of the phenoxy ring appeared to block the decarboxylation of 2,4-F in McIntosh leaves.

To investigate this possibility, tests were conducted with 2,4-F (*3*) similar to those previously carried out on 2,4-D. Carboxyl-labeled 2,4-F was prepared having a specific activity of 1 mc/mmole identical with the carboxyl-labeled 2,4-D which had been used in the earlier decarboxylation studies and with which it was compared. Equipment was assembled to supply apple shoots with dilute solutions of the two carboxyl-labeled compounds and to collect the $C^{14}O_2$ given off by the leaves. The shoots were cut from trees of the desired varieties and transferred immediately to small flasks containing the carboxyl-labeled solutions. These were then placed in large jars through which air could be drawn and the CO_2 absorbed in NaOH solutions. Light was excluded during the respiration periods in order to collect the maximum amount of CO_2 from the leaves. The carbonate was precipitated from the NaOH solution, and the precipitate was collected on filter paper for counting.

It was found that the decarboxylation of the 2,4-F-1-C^{14} occurs at a much slower rate in McIntosh leaves than does the decarboxylation of the 2,4-D-1-C^{14} (Table 1). In 24 hr only 4 percent of the C^{14} was recovered as $C^{14}O_2$ from the McIntosh shoots supplied with 2,4-F-1-C^{14}, while 33 percent of the C^{14} was recovered from the shoots supplied with 2,4-D-1-C^{14}. Even in Stayman, where decarboxylation of 2,4-D is extremely slow, the breakdown of the compound is further retarded by the substitution of the fluorine. Bioassays have shown that the decarboxylated form of 2,4-D is comparatively inactive.

Autoradiographs have been made of McIntosh and Stayman leaves treated with these carboxyl-labeled compounds. They show a rapid disappearance of C^{14} from McIntosh leaves supplied with 2,4-D-1-C^{14}. Similar leaves supplied with an equal amount of 2,4-F-1-C^{14} show much higher C^{14} activity. Thus it is apparent that 2,4-F may be absorbed by McIntosh leaves and move through the leaves to abscission sites without being inactivated.

Table 1. Production of $C^{14}O_2$ by apple leaves on detached shoots treated with 2,4-D-1-C^{14} and 2,4-F-1-C^{14}.

Treatment	Amount absorbed* (μg)	Absorbed C^{14} recovered as $C^{14}O_2$ (%)	
		4 hr	24 hr
	McIntosh		
2,4-D-1-C^{14}	40	3.25	33.04
2,4-F-1-C^{14}	45	0.43	4.13
	Stayman		
2,4-D-1-C^{14}	40	0.04	0.56
2,4-F-1-C^{14}	50	0.03	0.14

* After the 4-hr absorption period the shoots (8 leaves per shoot) were transferred to distilled water and the respiration run continued for an additional 24 hr.

Further evidence of the stability and effectiveness of 2,4-F in delaying abscission is its effect on the flowers. The application of 2,4-F either as dilute aqueous sprays or in a lanolin paste to flowers of several varieties including McIntosh was found to inhibit their abscission. In fact, it was observed in 1960 that nearly all of the flowers persisted throughout the summer on the McIntosh trees treated the previous fall with 2,4-F for control of preharvest drop, even though the proportion of flowers that formed mature fruits was reduced by the treatment (Fig. 1). This is similar to the stability of 2,4-D in Stayman. It has been reported (*4*) that Stayman trees sprayed with 2,4-D for delay of drop one year may show significant reduction in preharvest drop

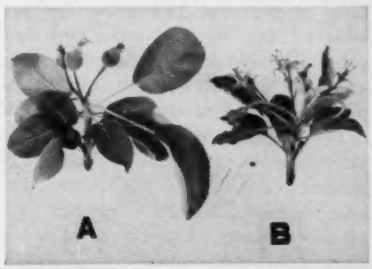

Fig. 1. Representative spur from untreated McIntosh tree (*A*) and from tree sprayed with 20 ppm 2,4-F (*B*). The spray was applied Sept. 1959; spurs were photographed 13 June 1960. Note the leaf distortions and persistent flowers on spur from treated tree. The leaf symptoms include enlargement of leaf veins, shortening and narrowing of the leaves, and development of marginal ruffles similar to the distortions produced by 2,4-D on susceptible varieties and species.

the following year without further application of 2,4-D. The substitution of fluorine in 2,4-D would appear to make it equally stable in varieties that otherwise decarboxylate it.

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3 April 1961

Variation in Clones of Penstemon Growing in Natural Areas of Differing Radioactivity

Abstract. A study to determine whether or not the relatively high radioactivity of a natural area has produced detectable morphological effects on plants of the species *Penstemon virens*, a plant of rather plastic morphology, has been conducted in the Central City region of Colorado for over 2 years. While no differences in kinds of anomalies were found to exist between plants growing in the sites of highest and lowest radioactivity, the number of anomalies was greater in plants from sites of greatest radioactivity.

A study was made of 26 clones of *Penstemon virens* growing along the crest of a dike of nonporphyritic quartz bostonite. The ground-surface gamma radioactivity varied from 0.05 to 0.40 mr/hr. According to Phair (*1*), this dike may be the most radioactive igneous rock known on the North American continent. Except in radioactivity, the microenvironments of the clones appeared to be quite similar.

Plant organs that are commonly known to be radiosensitive were examined and measured. The total heights and internodal lengths were measured on 206 flowering spikes; stage of development was determined on more than 4000 floral elements; and the total numbers of nodes, peduncles, and anomalies such as those shown in Fig. 1 were counted for each spike. Simultaneously the gross radiation environment of each clone was determined with a portable Geiger counter, and by securing segments of flowering spikes and selected samples of the adjacent soil for radioassay.

Preliminary analysis of the field data indicate several differences between clones: The range of morphological variability was greater, the percentage of aborted flowers was larger, the numbers of nodes per flowering spike were less, and the number of gross anomalies was higher in clones from the most radioactive sites; however, the average height, numbers of floral elements (buds, flowers, and fruit), and numbers of peduncles of the flowering spikes were very nearly the same in all sites.

Several hypotheses to explain the differences can be suggested: The differences may result from (i) chance, (ii) errors in measurement, (iii) slight variation in microenvironment (other than radioactivity), and (iv) variations in radioactivity. The first two hypotheses can be disregarded because of the large number of comparative measurements made. The several thousand measurements are the aggregates of measurements made by eight to ten different people, and approximately 75 percent of the measurements were independently double checked. Data placed in questionable and arbitrary categories (such as "immature or aborted") were disregarded.

Although the clones all appeared to be growing in similar microenvironments, the possibility exists that very subtle differences in amounts of light, temperature, insect damage, and moisture during critical periods of plant growth and differentiation could account for the differences between clones. It is known that gene action, even in the uniform environment of a single clone, can vary in expression. However, one observation suggests that this is not the reason for the differences in numbers of anomalies between the clones in this case. A study, in 1959, of *Penstemon* growing in a wide range of habitats provided evidence that soil drought, excessively high temperatures, and other environmental factors can account for various "anomalies" but that one of the first general effects of such factors is that the plant is somewhat stunted. In the present study the clones growing in the more radioactive sites were as tall as those in the less radioactive sites. Furthermore, clones from the habitats examined in 1959, including those of the extremely dry and exposed rock outcrop, never showed as many anomalies as the clones from the most radioactive habitats.

There is a final consideration. The radioactivity of the substrate is high compared with that of other natural areas, but alone it would probably be regarded by most radiobiologists as too low to cause detectable morphological

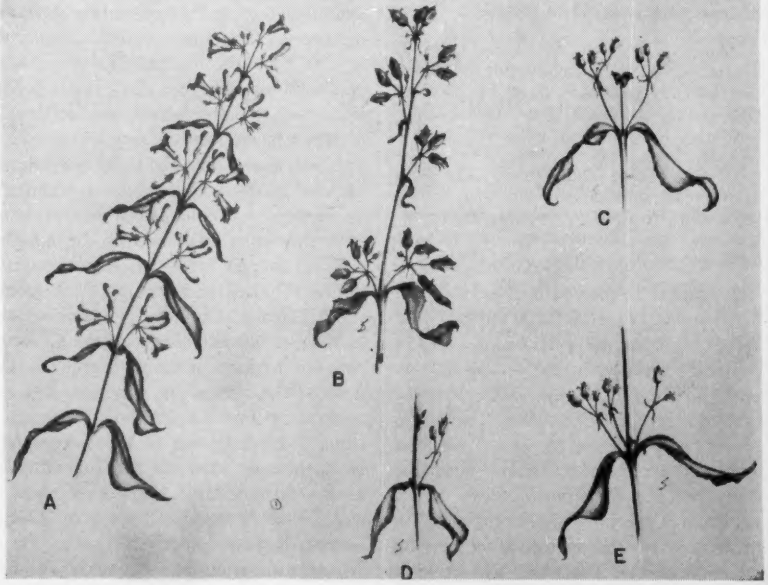

Fig. 1. (*A*) Typical flowering spike of *Penstemon virens*. Note opposite leaves, one axillary peduncle on each side of node, absence of aborted buds, and regularity of internodal lengths. (*B*) Spike has opposite and alternate arrangement of leaves and several aborted buds near the top. (*C*) Terminal development incomplete. (*D*) Blocked development of one peduncle and fragmentary nodal development. (*E*) Extra peduncle.

effects. In ecology there is a commonly accepted principle which is worthy of serious consideration in this situation: If conditions are less than optimum for an organism with respect to one ecological factor, the sensitivity of the organism to other factors may be increased. There is ample evidence that some environmental "stress" factors, especially suboptimum amounts of oxygen and abnormal temperatures, increase the sensitivity of plants to radioactivity (see *2*). Therefore, at the present time the most tenable hypothesis appears to be that background radioactivity, acting in conjunction with other suboptimum environmental factors, is responsible for the greater incidence of anomalous morphological forms (*3*).

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13 April 1961

Enzymatic Formation of Psychotomimetic Metabolites from Normally Occurring Compounds

Abstract. An enzyme has been found that N-methylates serotonin and tryptamine to psychotomimetic metabolites, bufotenine and N,N-dimethyltryptamine. This enzyme is highly localized in the rabbit lung and also N-methylates phenylethylamine derivatives such as tyramine, phenylethylamine, mescaline, and dopamine.

In recent years, there has been an active search for a biochemical cause of mental disease. Several compounds have been reported to be present in the body which produce abnormal behavior, but in rigorously controlled studies none of these findings have been confirmed (*1*). Cohoba, a snuff obtained from *Piptadenia peregrina*, has been used by Indian tribes of Haiti to enable them to communicate with unseen powers. Recently, bufotenine (N,N-dimethylserotonin) and N,N-dimethyltryptamine have been found to be present in *Piptadenia peregrina* (*2*), and both of these compounds have been shown to produce psychotomimetic effects in man (*3*). I wish to report that an enzyme has been found in the rabbit lung that can convert the normally occurring compounds, serotonin and tryptamine, to the psychotomimetic metabolites, bufotenine and N,N-dimethyltryptamine.

When the methyl donor S-adenosylmethionine-methyl-C^{14} (C^{14}AMe) was incubated with the soluble supernatant fraction of rabbit lung, a normally occurring compound present in this tissue became radioactive. In trying to characterize this substance, it was found that, when serotonin was incubated with the soluble supernatant fraction of rabbit lung and C^{14}AMe, considerable amounts of a radioactive compound were formed. This derivative could be extracted into isoamyl alcohol at *p*H 10. After chromatography with three solvent systems—butanol, ethanol, and ammonia (8:2:1), *n*-propanol and ammonia (1*N*) (5:1); and isopropanol, ammonia, and water (16:1:3)—the radioactive compound formed from serotonin and C^{14} AMe had the same R_F values as authentic N-methylserotonin. When N-methylserotonin was incubated with C^{14}AMe and the rabbit lung enzyme preparation, a compound was formed having the same R_F values as bufotenine in several solvent systems. In addition, typtamine and N-methyltryptamine, when incubated with C^{14}AMe and the enzyme from rabbit lung, formed radioactive metabolites having the same R_F values as N-methyltryptamine and N,N-dimethyltryptamine, respectively, when chromatographed on Whatman No. 1 paper buffered at *p*H 8.0, with *n*-butanol or isoamyl alcohol saturated with water as the solvent systems. These compounds were isolated from the enzymatic reaction mixture by extraction into isoamyl alcohol at *p*H 10. The relative rates of enzymatic formation of the N-methylated derivatives are shown in Table 1. These observations were taken as evidence that serotonin and tryptamine are converted to their corresponding N-dimethyl derivatives by an enzyme present in the soluble supernatant fraction of the rabbit lung in two steps as follows:

$$\text{serotonin} \xrightarrow{\text{AMe}} \text{N-methylserotonin} \xrightarrow{\text{AMe}} \text{bufotenine}$$

$$\text{tryptamine} \xrightarrow{\text{AMe}} \text{N-methyltryptamine} \xrightarrow{\text{AMe}} \text{N,N-dimethyltryptamine.}$$

Table 1. Enzymatic N-methylation of indoleamines. Rabbit lung was homogenized with three volumes of isotonic potassium chloride and centrifuged at 80,000 *g* for 30 min. Soluble supernatant fraction obtained from 15 mg of rabbit lung was incubated at 37°C with 10 mμmole of S-adenosylmethionine-methyl-C^{14}, 100 μmole of phosphate buffer at *p*H 7.9, and 0.5 μmole of substrate. After 90 min of incubation, the methyl-C^{14} indoleamine was determined in the incubation mixture (*4*).

Substrate added	Product formed	
	Name	Amount (μg/g of tissue)
Serotonin	N-Methylserotonin	80
N-Methylserotonin	Bufotenine	56
Tryptamine	N-Methyltryptamine	71
N-Methyltryptamine	N,N-Dimethyltryptamine	20

This enzyme was also found to N-methylate other phenylethylamine derivatives such as phenylethylamine, tryamine, mescaline, and dopamine (*4*); and it appeared to differ from other N- and O-methyltransferases with regard to substrate specificity and distribution (*5*).

Recently, Pollin *et al.* (*6*) found that the repeated oral administration of large amounts of *l*-methionine and *l*-tryptophan caused marked alterations of behavior in schizophrenic patients. Both of these amino acids can serve as precursors for the psychotomimetic compounds, bufotenine and N,N-dimethyltryptamine.

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6 April 1961

Histochemical Demonstration in Rat of Monoamine Oxidase Inhibition by β-Phenyl-Isopropyl Hydrazine

Abstract. A histochemical method for demonstration of monoamine oxidase activity was found to be almost as sensitive as a biochemical method when used for revealing total inhibition of monoamine oxidase in rat tissues after administration of β-phenyl-isopropyl hydrazine. The histochemical method is of special value in the study of monoamine oxidase inhibition in the complex structures of the brain.

β-Phenyl-isopropyl hydrazine is a very potent monoamine oxidase inhibitor. In the rat, Horita (*1*) demonstrated biochemically total inhibition of monoamine oxidase in pooled brain samples after a dose of $5 \times 10^{-6} M$ β-phenyl-isopropyl hydrazine per kilogram of body weight. To our knowledge, no attempts have been made to locate monoamine oxidase inhibition in rat tissues. The histochemical tetrazolium method of Glenner *et al.* (*2*) was found to be sensitive enough for this purpose.

Female albino rats of the Wistar strain, weighing 160 to 200 g, were used in the experiments. β-Phenyl-isopropyl hydrazine (*3*) was dissolved in water to different concentrations so that 0.1-ml solutions injected intraperitoneally contained doses ranging from 1×10^{-8} to $5 \times 10^{-7} M$/kg body weight. After 6 hours, the rats were killed by decapitation. Brain, liver, and kidney were rapidly removed and frozen with carbon dioxide snow on metal blocks together with a corresponding control specimen. Untreated litter mates, and in some experiments also rats treated with equimolar doses of iproniazid and nialamide, served as controls. In a cryostat 10-μ sections were cut simultaneously, picked up on coverslips, and incubated at 37°C for 45 minutes with Nitro-Blue tetrazolium as electron acceptor and tryptamine as substrate (*2*).

In the brain of the control rats, the distribution of monoamine oxidase corresponded well with the observations of Shimizu *et al.* (*4*). In the rats treated with β-phenyl-isopropyl hydrazine, the monoamine oxidase of brain was totally inhibited even by a concentration of $5 \times 10^{-6} M$/kg (Fig. 1, top). The locus coeruleus, which is the most strongly active nucleus in the rat brain (*4*), however, retained a moderate activity.

In the liver and kidney, monoamine oxidase inhibition was total after administration of β-phenyl-isopropyl hydrazine in a dose of $4 \times 10^{-5} M$/kg (Fig. 1, bottom). At a concentration of $2 \times 10^{-5} M$/kg, the periportal areas of the liver lobules retained traces of activity, the central areas being inactive. At this concentration, the straight terminal portions of the proximal convoluted kidney tubules exhibited a faint staining.

In the demonstration of total monoamine oxidase inhibition, the histo-chemical tetrazolium method appears to be almost as sensitive as the spectrophotometric method used by Horita (*1*). In the brain, both methods revealed complete inhibition at the same dosage of β-phenyl-isopropyl hydrazine, whereas in the liver there was a slight difference in favor of the biochemical method.

Consequently, the histochemical method offers an excellent tool for the localization of monoamine oxidase inhibition in the complex structures of the brain. It is known that the various substrates of monoamine oxidase are concentrated in different parts of the brain (*5*). Moreover, monoamine oxidase inhibitors are selective in their action, causing differences in the amounts of individual monoamines accumulated in pooled brains (*6*). This may be because of differences in the distribution of the monoamine oxidase inhibitors in the brain, which, in turn, could be a consequence of their dissimilar chemical structure (*7*).

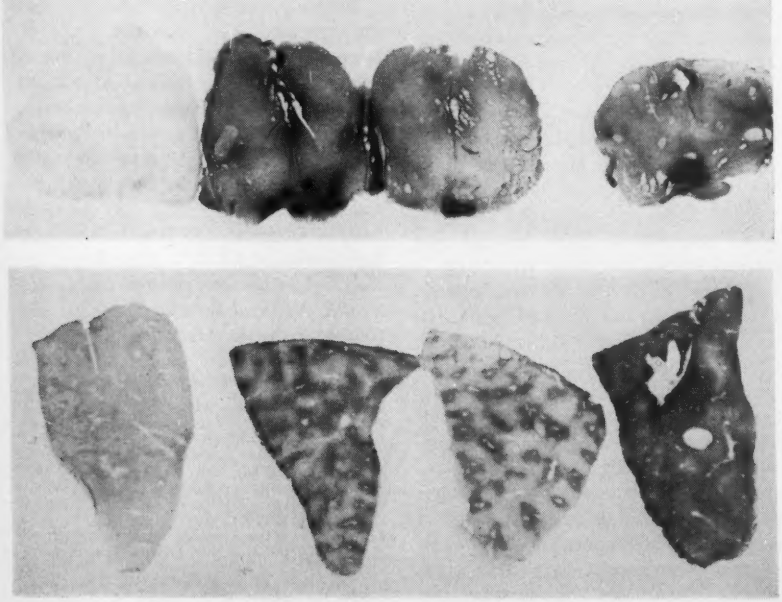

Fig. 1. Top, Vertical cross sections of the rat pons. From left to right: untreated control, and animals 6 hours after administration of iproniazid, nialamide, and β-phenyl-isopropyl hydrazine in a dose of $5 \times 10^{-6} M$/kg, respectively. Note the total inhibition after administration of β-phenyl-isopropyl hydrazine. Bottom, Liver of rat. A similar arrangement, but a higher dose of $2 \times 10^{-5} M$/kg. Note the subtotal inhibition caused by β-phenyl-isopropyl hydrazine and the centrolobular inhibition caused by iproniazid.

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9 January 1961

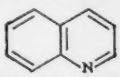
Kodak reports on:

memories of Skraup . . . Mr. Burnham's pitch on randomness . . . cutting down on copy breaks

Plenty of good, clean quinoline

We have always loved to run that most wonderful of "name" reactions, the Skraup.

We can remember when we were younger lugging those 22-liter flasks. We distinctly remember that they weighed 76 pounds because we remember weighing one out of curiosity one day. It occurs to us now that we were stronger and luckier than we were smart. A little slip while wrestling that much hot sulfuric acid would have been bad for our complexion. Other ingredients of Skraup brew were aniline, glycerine, and nitrobenzene. The sulfuric acid dehydrates the glycerine to acrolein, the acrolein cyclizes against the benzene ring of the aniline, the sulfuric acid grabs off a third molecule of water, and the nitrobenzene oxidizes off two hydrogen atoms. The chain of events starts quietly enough but picks up considerable exothermic enthusiasm. Result: quinoline,



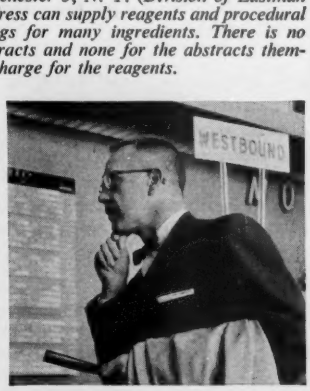
It was an exhilarating affair, particularly when we succeeded in pushing the yield close to 100%. Then we passed 100%, which was even more exhilarating. This we explained by assuming that the nitrobenzene was being reduced to more aniline for participation in the reaction. (Zdenko Hans Skraup would have been justifiably provoked with us for tortuous reasoning. His original proposal was merely to react nitrobenzene, glycerine, and sulfuric acid. Later, aniline was included.)

Anyway, we took pride in the efficiency with which we could furnish the world plenty of good, clean quinoline, a compound once considered the foulest of coal-tar derivatives.

Now it appears that good, clean quinoline is going to be needed more than ever. A new analytical method for determination of phosphorus in fertilizers is based on the discovery that quinolinium phosphomolybdate ($(C_9H_7N)_3$-$H_3PO_4 \cdot 12MoO_3$) is of constant composition, very insoluble, and free of occluded cations.

A free procedural abstract and the quinoline come from Distillation Products Industries, Rochester 3, N. Y. (Division of Eastman Kodak Company). Same address can supply reagents and procedural abstracts to test many things for many ingredients. There is no charge for a list of the abstracts and none for the abstracts themselves, but there is a slight charge for the reagents.

Surviving platemaker



Meet J. Mason Burnham, a brisk-looking Kodak man who has a problem. Mr. Burnham sounds off like this:

"Characteristically, the random shift in position of an image on a Kodak photographic plate is between 0.9 and 1.4 microns. Random, mind you.

"Positional error which is not random can be corrected. The correcting equations can be cranked into the computation program along with all the other computations. A lot of computation has to be done in any event when they measure the missile trail and the star trails on the plates from a whole string of ballistic cameras along a range.

"Randomness is the only ultimate limitation on precision in such a situation. The magnitude of the random component of physical shift of an image on a plate between exposure and measurement is not great in comparison with the magnitude of the errors in all the other quantities that enter into the computation. Small as the random shift is, it is well that we now have a pretty good idea of its size.

"Among transparent materials which can carry an image-bearing emulsion, glass is the only one that has zero humidity expansion coefficient. Of course, its thermal expansion coefficient is less than that of any film base and even less than that of hardened steel. This stability can be handy when you don't have a computer available to remove non-random errors.

"As for flatness, we have recently started accepting special orders for all Kodak plates on ¼-inch micro-flat glass, which means that the surface bearing the emulsion is planar to 0.2 micron per centimeter, for sizes from 4 in. x 4 in. to 12 in. x 12 in."

Mr. Burnham, as noted above, has a problem. The photographic plate was the product with which our founder started his one-man business. Mr. Burnham's problem is to keep this original rootstock of the business thriving despite all the competition for attention that the intervening 81 years have brought. He is going about it through contributions to modern instrumentation. If you would like to ask any questions about Kodak plates for instrumentation—for example, how to process a plate complete to dryness in 10 minutes without much spoiling the spatial stability of the image—write Eastman Kodak Company, Special Sensitized Products Division, Rochester 4, N. Y.

Has anybody seen Gwendolyn?

Lucky is the scientific worker who can afford a contemptuous attitude toward office routines. This item will bore him.

It deals with those copying machines that are now seen wherever there is paperwork. Their popularity is traceable to the introduction of the *Kodak Verifax* copier some 8 years ago. Now there are dozens upon dozens of makes of office copiers. The Verifax copier differs from the other inexpensive ones in permitting as many as five copies to be run off from a single sheet of sensitized material. The cost of making n copies is therefore $c_V = s_V + np_V$ where s_V is the cost of the sensitized material (which we call—and don't take this too hard—the "magic matrix") and p_V is the cost of a sheet of copy paper. With the others, the cost of making n copies is simply $c_A = n\ s_A$.

Here are some going rates for Verifax and other systems:

s_V	p_V	s_A	s_B	s_C	s_D
8¢	1¢	8¢	7¢	6¢	5¢

On this basis it becomes clear that if more than one copy is usually required, the Verifax copy is the best buy.

There are copiers which need no expendable sensitized goods. The cost or rental fee for these machines generally confines them to a central location where they can serve an entire organization of some size. This leads to the question of the reason for having a secretary. If you need her merely as a status symbol, we have nothing further to say to you on this subject. If, though, she has more directly useful work to do that justifies a weekly salary of $70 and she averages three 10-minute trips a day to the central copier, her walks for copies cost $225 a year. A Verifax copier could be placed next to her desk for less than $100.

Simple though these great economic truths may be, we have gone so far as to prepare little cardboard calculators for convenience in making representations to the management. Request a free set from Eastman Kodak Company, Business Photo Methods Division, Rochester 4, N. Y.

Price subject to change without notice.

Kodak

TRADE MARK

This is another advertisement where Eastman Kodak Company probes at random for mutual interests and occasionally a little revenue from those whose work has something to do with science

Meetings

Oceanography in the Midwest

A two-day symposium on Oceanography in the Midwest, a discussion of ways and means to expand the nation's oceanographic research and educational programs, was held on the University of Wisconsin campus, 15–16 May. The symposium was an outgrowth of President Kennedy's public recognition, in two major speeches, of the importance of oceanography, from the point of view both of scientific development and of national defense.

The meetings began with an address by Conrad A. Elvehjem, president of the University of Wisconsin, who stressed the need for expanded research programs. It has become one of our national goals, he said, to obtain a vastly improved understanding of the seas around us, and increased knowledge of oceanography can serve both to link us in a common bond with other nations and to serve as a bulwark in our defense.

There were more than 100 participants, from the nation's oceanographic stations along the Atlantic and Pacific coasts, from federal agencies, and from universities of the Midwest. The symposium was sponsored by the U.S. Office of Naval Research, the National Science Foundation, and the Committee on Institutional Cooperation of the Council of Ten and the University of Chicago.

During the first morning of the symposium some of the nation's leading oceanographers described the research activities and educational curricula under way or planned at the oceanographic laboratories and discussed the part the Midwest may play in these programs.

Richard H. Fleming of the University of Washington said the really challenging problems of the future go beyond mapping and measuring. The United States now needs to know more about the processes at work in the oceans, the heat budgets, the reasons why the sea behaves as it does.

Fritz Koczy of the University of Miami added that measuring oceanographic phenomena was only the first step; "then must come the theoretical work to explain the questions which arise from the data obtained. . . . These questions can be answered in the Midwest as well as they can at the sea's edge."

Paul M. Fye of the Woods Hole Oceanographic Institution noted that one problem encountered in training oceanographers in the Midwest is that of giving students opportunities for training aboard seagoing vessels. Cooperative programs should be worked out with oceanographic institutions in order to give training at sea as part of the curriculum in oceanography of midwestern universities, he said. Travel is now so easy and rapid that this is no longer a serious problem, but coastal stations will require expanded facilities to accommodate larger numbers of students.

The afternoon was devoted to presentations of papers by scientists of the Midwest who are currently conducting research either in the oceans or in lakes. Arthur D. Hasler of the University of Wisconsin reviewed research that has been done in small lakes in Wisconsin and cautioned that national oceanographic programs should certainly include expansion of work on the inland lakes that may serve as models for experimental oceanography.

John C. Ayers of the University of Michigan pointed out that the Great Lakes offer an excellent training ground for oceanographers. "Most of the influences which are studied in the oceans are equally available in the Great Lakes," Ayers said. Reid A. Bryson of the University of Wisconsin added that lakes are models of the sea and that research into many aspects of oceanography can be conducted most readily in small bodies of water.

Robert Miller and Ralph Johnson of the University of Chicago described the cooperative programs worked out between the University of Chicago's department of geophysical sciences, the Woods Hole Oceanographic Institute, and the Pacific Marine Station. This program provides for an exchange of professors and for space at the coast-based institutes during the summer months.

Programs in oceanography of the National Science Foundation, the Office of Naval Research, and the National Institutes of Health were presented on the second day of the symposium. This presentation was followed by a panel discussion, in which the audience participated, on ways and means to expand research and training programs in the Midwest.

Willis E. Pequegnat, associate program director of the National Science Foundation, outlined the Foundation's educational programs. George Sprugel, Jr., NSF's program director for environmental biology, stressed the willingness of his division to support valuable programs regardless of geographic location.

John Lyman, associate program director for earth sciences (oceanography), National Science Foundation, and Irving Gerring, executive secretary of the environmental sciences and engineering study section, National Institutes of Health, described the workings of their organizations.

Arthur E. Maxwell, head of the geophysics branch, Office of Naval Research, outlined an expanded 10-year oceanographic program to be carried on by the Navy and stated that funds will be available to institutions for supportive work.

The panel discussion was led by George Woollard, University of Wisconsin, who, in a lecture the previous evening, had surveyed our present knowledge of the earth's crust.

An informal poll made at the symposium showed that many students have asked for training in oceanography at universities of the Midwest and that many more such requests are anticipated. The symposium participants agreed that midwestern institutions can make a significant contribution if coastal facilities are made available.

LOUIS S. KORNICKER
U.S. Office of Naval Research, Chicago, Illinois

Forthcoming Events

August

28–31. Botanical Soc. of America, Lafayette, Ind. (B. L. Turner, Dept. of Botany, Univ. of Texas, Austin 12)

28–2. Mechanics of Turbulence, intern. colloquium, Marseilles, France. (A. Favre, Faculté des Sciences, Université, Marseilles)

29. American Soc. for Horticultural Science, Lafayette, Ind. (R. E. Marshall, Dept. of Horticulture, Michigan State Univ., East Lansing)

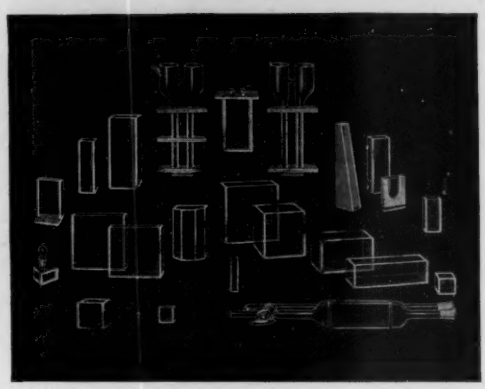
29–1. American Mathematical Soc., 66th summer meeting and 40th colloquium, Stillwater, Okla. (J. W. T. Youngs, AMS, 190 Hope St., Providence 6, R.I.)

29–1. Society for Industrial and Applied Mathematics, Stillwater, Okla. (G. Kaskey, Remington Rand UNIVAC, P.O. Box 500, Blue Bell, Pa.)

29–6. Planning of Experiments, intern. colloquium, Paris, France. (D. Dugue, Institut de Statistique de l'Université, 11 rue Pierre Curie, Paris 5)

29–7. International Statistical Inst., 33rd session, Paris, France. (G. R. Chevry, 29 Quai Branly, Paris 7)

GLASS ABSORPTION CELLS made by KLETT



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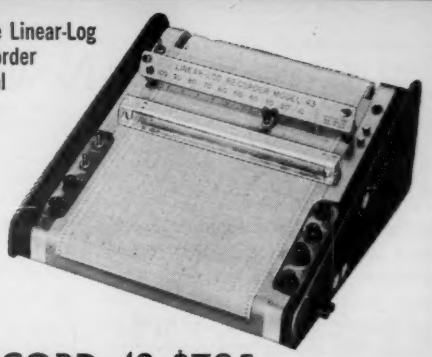

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PHARMACOLOGISTS-TOXICOLOGISTS

Armour Research Foundation has openings for high calibre research personnel with experience or advanced degrees in drug metabolism or tracer methodology, or experience in systemic effects or effects of toxic materials.

These positions require men with Ph.D.'s or Masters Degrees in Pharmacology, Biochemistry or Pharmacology-Toxicology.

We are expanding our staff in this area and have many interesting and varied research programs. You will have an opportunity to work in small project groups with some of the leading scientists in these fields. We are located in metropolitan Chicago which offers many cultural advantages. Excellent employee benefits including a very liberal vacation. All qualified applicants will receive consideration for employment without regard to race, creed, color or national origin.

Please send complete resume and salary requirements to E. B. Beck.

ARF

ARMOUR RESEARCH FOUNDATION
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NOW...MECHANICALLY, COTTON PLUG UP TO 2400 PIPETTES PER HOUR

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HARRISON PIPETTE PLUGGER

- Cotton plugs pipettes up to 2400 per hour
- Consistently uniform cotton plugs
- Versatile—accepts full range of standardized cotton plugging pipettes without adjustment
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- Compact—requires little floor space

The Harrison Pipette Plugger eliminates the slow, tedious job of hand stuffing cotton in pipettes. An experienced operator can plug pipettes up to 2400 per hour, with each cotton plug absolutely uniform in size. Cotton plugging speeds adjustable to 22, 30 or 40 pipettes per minute. The Harrison Pipette Plugger can be used over a full range of standardized cotton plugging type pipettes *without adjustment*, including the following pipettes: Bellco V.I.P: 12-334, Corning 7086, and Kimble 37034A. Other pipettes having identical top dimensions and tolerances as these will also be satisfactory. However, conventional pipettes can be reworked and shaped to the cotton plugging top dimensions . . . if they are of borosilicate glass.

The Harrison Pipette Plugger is mounted on a sanitary work surface featuring a semi-enclosed base. A shelf beneath the table holds the cotton roving, which is fed through a special opening in the table.

WRITE FOR BULLETIN NO. P-50-15

BELLCO GLASS INC. VINELAND, N.J.

New Products

Nuclear magnetic-resonance spectrometer is designed for qualitative and quantitative proton analysis. The spectrometer control console includes the radio-frequency transmitter and receiver that excite the sample and receive the resulting nuclear magnetic-resonance signal. The console also includes components of a field- and frequency-control circuit that maintains the proper relationship between the magnetic field and the effective transmitter frequency in spite of variations in magnetic field strength. The control circuit utilizes a reference sample incorporated in the feedback loop of the excitation oscillator. The reference sample and the analytical sample are located adjacent to each other and are excited by the same radio-frequency and modulation fields. The magnet system includes a 6-in., 14,092-gauss magnet with a water-cooled solid-state power supply. Magnetic-field homogeneity control coils are provided as well as means for spinning the analytical sample in the probe. An integrator included in the system makes available both qualitative and quantitative information. The instrument's flat-bed recorder allows recording of either the spectrum or its integral on precalibrated chart paper.

Manufacturer's specifications of the spectrometer include: operating frequency, 60 Mcy/sec; radio-frequency field at the sample, approximately 0.02 to 2.0 mgauss; typical sample volume, 0.2 to 0.4 cm^3; sample-tube outside diameters, 5 mm; resolution, defined as line width at half-maximum amplitude, 0.6 cy/sec; integral accuracy, ±2 percent when integrating spectra; maximum rate of change of field homogeneity during normal operation, 1 cy/sec per hour. (Varian Associates, Dept. Sci258, 611 Hansen Way, Palo Alto, Calif.)

The information reported here is obtained from manufacturers and from other sources considered to be reliable. Neither Science *nor the writer assumes responsibility for the accuracy of the information. All inquiries concerning items listed should be addressed to the manufacturer. Include the department number in your inquiry.*

Probe positioning system that may be used to position a probe in an electrolytic tank is similar in operation to an *x-y* recorder. The system operates from a voltage input to position the probe head anywhere within a 42- by 58-in. area. The head provides vertical and horizontal mounting surfaces useful for mounting probes or other special devices weighing up to 30 lb. Traverse speeds up to 6 in./sec are obtained with a maximum positioning error said to be 0.05 in. Servo amplifiers and power supplies are separate from the main frame and are suitable for rack mounting. (Benson-Lehner Corp., Dept. Sci.254, 1860 Franklin St., Santa Monica, Calif.)

Travel indicator measures motion by means of a gage wheel contacting a way or machined surface. Motion is transmitted through two trains to a dial indicator reading in thousandths. A dial knob graduated in inches and tenths of an inch gives a continuous record for up to 6 in. of travel, repeating thereafter on any length of traverse. A slip clutch permits zero adjustment without disengaging the gage wheel. Accuracy is said to be 0.001 in. in 6 in. of travel. (Southwestern Industries, Inc., Dept. Sci256, 5880 Centinela Ave., Los Angeles 45, Calif.)

Carbon-hydrogen analyzer is an automatic apparatus for application of the Pregl method of analysis. The instrument will analyze substances pyrolizing at temperatures under 1100°C. For routine analysis, results are said to correspond to theory within ±0.2 percent of carbon and hydrogen. Usual sample size is 5 to 50 mg. The instrument's complete cycle requires 9 min. Furnace controls permit selection of combustion temperature from 700° to 1000°C. An auxiliary timer permits a 5-min extension of combustion period for difficult materials. (Coleman Instruments Inc., Dept. Sci275, 42 Madison St., Maywood, Ill.)

Frequency-deviation meter is said to be capable of measuring and recording frequency deviation of one part in 10^{10} with full-scale deflection for a frequency difference of one part in 10^9. The instrument consists of a frequency comparator and a recorder. The comparator compares the output of a 0.1-, 1.0-, 2.5-, or 5.0-Mcy/sec secondary frequency standard with the output of primary frequency standards. Indication of frequency deviation is provided by observation of Lissajous figures. For recording purposes a d-c output proportional to frequency deviation and a counter output for direct reading are provided. The comparator contains 16 transistorized modules including a regulated power supply. The recorder consists of a zero-center galvanometer, a recording-pen system, a chart carriage, paper drive and takeup motors. Paper speeds are 12, 6, 3, 1.5, 0.75 in./hr or in./min. (Aircraft Radio Corp., Dept. Sci273, Boonton, N.J.)

Electromagnet provides a field intensity of 20,000 gauss over a 64-in. area with 1.5-in. gap. Standard pole-face geometry is a 4- by 16-in. rectangle. Pole faces are soft steel or Inconel. Magnet coils are wound with copper ribbon insulated with class-B materials. The complete magnet assembly measures 46 by 38.5 by 42 in. and weighs 4 tons. (MHD Research, Inc., Dept. Sci266, P.O. Box 1815, Newport Beach, Calif.)

Magnetic-drum memory can be read while the drum is stationary and while it is rotating. Size of the drum varies with the quantity of information to be recorded. A ten-channel, 2000-bit drum measures 26 by 14 in., including heads and terminal board. Output from the drum has sufficient power to eliminate the need for sensitive amplifiers. Output into 1000 ohms is 1.5 volts d-c for a "one" reading and less than 30 mv for a "zero" reading. Into a cold-cathode matrix, drums may have an output of 65 volts a-c for "one" and less than 2 volts for "zero." The memory device is designed especially for machine-tool control. For this application, coordinates for each cutting operation are recorded as a series of parallel binary code words on sequential steps of the drum. (Consolidated Controls Corp., Dept. Sci264, Bethel, Conn.)

JOSHUA STERN
National Bureau of Standards, Washington, D.C.

PERSONNEL PLACEMENT

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Single insertion	$40.00 per inch
4 times in 1 year	38.00 per inch

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Replies to blind ads should be addressed as follows:
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POSITIONS WANTED

Biology Teacher desires position in northern college. M.A.; now teaching zoology, botany, plant morphology; trained in zoology, ecology, conservation. Publications; references available. Daniel McKinley, 624 Hunter Avenue, Winston-Salem, North Carolina. 8/4

Cell-research Methodologist and coordinator interested in appointment in medical school department developing research and training programs on cells, viruses, cancer. Box 164, SCIENCE. X

Plant Pathologist. B.S., M.S.A. 2 years' experience field research sugar industry; 4 years' with U.S. Department of Agriculture. Box 160, SCIENCE. X

Zoologist-Physiologist. Ph.D. 38. Desires academic position. Nine years' teaching. Publishing. Available June 1962. Attending August AIBS meetings. Box 163, SCIENCE X

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—with broad biological background; able to work effectively with both top scientific and managerial personnel. Must possess strong facility in oral and written communication. Experience in pharmaceutical industry highly desirable. Ability to speak foreign language very helpful but not essential.

THE JOB

—to seek out potentially useful therapeutic compounds from sources outside our own laboratories and to preliminarily evaluate these agents with laboratory scientists representing all biological disciplines. Good opportunity for domestic and foreign travel and attendance at appropriate scientific meetings.

Send complete résumé including salary requirements to:

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For selective textbook program of established scientific publishers. Previous experience in planning and supervising college travellers' activities essential. Must have strong scientific background. Excellent salary.

Box 166, SCIENCE

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Large midwestern pharmaceutical firm needs young man to assume responsible role in tropical disease research group. New drug agents currently being sought in fields of amebiasis, shistosomiasis, oxyuriasis, intestinal worms, etc. Experience desirable but not necessary. Applicant must be willing and able ultimately to assume both technical and administrative duties of project leadership. Write, sending complete résumé and bibliography to:

P.O. Box 1047
Ann Arbor, Michigan

LABORATORY TECHNICIANS

For expanding slide department of biological supply company. Training in botanical technique and/or whole mount preparation required. Will consider short-term employment (2 years) as well as permanent employment. Salary commensurate with education, training, and experience. Excellent working conditions, suburban area, employee benefits, paid holidays and vacation, opportunities for advancement.

Box 162, SCIENCE

POSITIONS OPEN

UNIVERSITY OF MELBOURNE

Applications are invited for the position of **Reader in Human Genetics** in the Department of Zoology (Head: Professor M. J. D. White, F.R.S.). This is a new position made possible by the J. N. Peters Bequest. It is intended that the Reader should occupy space in the new wing of the zoology department, at present under construction, and which will be completed in the first half of 1962. Facilities for biochemical genetics, cytogenetics and a radioisotope laboratory will be available is this building. He would work in close association with the medical departments of the university and some of his teaching would be to students of the faculty of medicine. Secretarial and technical assistance would be provided and a basic grant for equipment would be available.

The present salary range is £A2,950-£3,250 (£3050-£3350 for a medically qualified Reader). Initial salary will be determined according to qualifications and experience. Superannuation is on the F.S.S.U. basis.

Further particulars and conditions of appointment may be obtained from the Registrar, University of Melbourne, Parkville, N.2., Victoria, Australia, and applications should reach him by October 15, 1961.

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Chemistry background. Expanding international scientific book publishing house. M.S. degree essential; Ph.D. advisable. Highest salary.

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Ph.D. versed in colloidal chemistry, for fundamental research in animal diseases, salary $7000–$8000. Reply: E. A. Tunnicliff, Head

Montana Veterinary Research Laboratory
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Leatherhead, Surrey, England

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Scientists who are suitably qualified for directing research work in this field are invited to apply for the post.

The salary will be in the region of £4,000 per annum in accordance with qualifications and experience. A contributory superannuation fund is in operation.

Applications should be addressed to The President, Professor A. C. Frazer, M.D., D.Sc., F.R.C.P., at the Laboratories of the B.F.M.I.R.A., Randalls Road, Leatherhead, Surrey, England, and should arrive not later than Friday, 1st September, 1961.

POSITIONS OPEN

POSITIONS OPEN

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ANIMAL PATHOLOGY RESEARCH
WITH THE
CANADIAN DEPARTMENT OF AGRICULTURE
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Candidates must be graduates in Veterinary Medicine from a university of recognized standing and have demonstrated interest in, and aptitude for, research.

For full details and application forms write to the CIVIL SERVICE COMMISSION OF CANADA, OTTAWA. Please ask for Information Circular 61-22.

The University of Saskatchewan invites applications for the position of Assistant Professor of Biology, effective July 1, 1962, at a minimum salary of $7000.00. Duties include undergraduate teaching in general biology and a program of research and graduate teaching in Limnobiology. Facilities in this field are excellent. Applications, including curriculum vitae, names of references, and a recent photograph, should be addressed to Dr. M. Shaw, Head, Department of Biology, University of Saskatchewan, Saskatoon, Saskatchewan, Canada.

CLINICAL MICROBIOLOGIST

Ph.D. preferred to supervise microbiology laboratory of large general hospital located in New York City. Opportunity for professional growth, research encouraged, university affiliation, salary about $9000 annually with liberal extras. Contact: Chief, Laboratory Service, Veterans Administration Hospital, 130 West Kingsbridge Road, Bronx 68, New York.

M.S. in Chemistry interested in working for Ph.D. in biochemistry at University of Houston. Identification and purification of biologic immune factor anti-tumor agent applied toward research requirements. Salary $6000-$7000. Box 20065, Houston 25, Texas.

BIOCHEMIST

Midwestern medical school department of medicine. Research and teaching in connective tissue. Ph.D. Salary and position commensurate with qualifications.

Box 161, SCIENCE

RADIOBIOLOGIST EXPERIENCED

Research and development on biological effects of ionizing radiation for application in long range biological control program. Knowledge of dosimetry required. Background in entomology and/or invertebrate zoology highly desirable. Write Director, Instituto Venezolano de Investigaciones Cientificas, Apartado 1827, Caracas-Venezuela.

MEMORIAL UNIVERSITY OF NEWFOUNDLAND

St. John's, Newfoundland, Canada

Applications are invited for the position of Assistant Professor of Biology to give instruction primarily in Animal Physiology.

Candidates with background and experience in Marine Biology will receive preference. Ph.D. or equivalent essential. Duties beginning September 1961 to include teaching and research. The starting salary will be based on qualifications and experience.

Applications accompanied by complete curriculum vitae and the names of three references should be addressed to the Head, Department of Biology, Memorial University of Newfoundland.

REGISTRAR

A.S.C.P. approved school of medical technology, large general teaching hospital affiliated with Western Reserve University, and Research Technician position—divide time. School duties include supervision of students, some teaching and recruitment. College graduate, major fields chemistry and biology, good salary, many benefits. Send résumé to Personnel Office,

Cleveland Metropolitan General Hospital
3395 Scranton Road, Cleveland 9, Ohio

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With experience in isolation of drugs and toxic substances, for toxicology laboratory. Starting salary $6480; $6920 at end of first year, maximum at $7640. Paid hospital and medical insurance. Send résumé to B. Dearington, State Department of Health, State Office Building, Hartford, Conn.

VIROLOGIST

To plan and conduct investigational, diagnostic, base-line and surveillance studies of viruses and related organisms in the Hawaii state public health laboratory. Requires 2 years' experience in propagating, detecting, and identifying viruses and completion of graduate work leading to a Ph.D. in virology, bacteriology, or a related field. Salary $8256–$10,536 per annum. Write to Department of Personnel Services, 825 Mililani Street, Honolulu 13, Hawaii.

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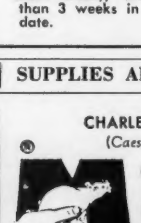

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2. The 29th John Wesley Powell Memorial Lecture. Speaker: Glenn T. Seaborg; Paul M. Gross, presiding.
3. On "AAAS Day," the four broad, interdisciplinary symposia—Physics of the Upper Atmosphere; Geochemical Evolution—The First Five Billion Years; Existing Levels of Radioactivity in Man and His Environment; and Water and Climate—arranged by AAAS Sections jointly.
4. The Special Sessions: AAAS Presidential Address and Reception; Joint Address of Sigma Xi and Phi Beta Kappa by Harrison Brown; the Tau Beta Pi Address; National Geographic Society Illustrated Lecture; and the second George Sarton Memorial Lecture.
5. The programs of all 18 AAAS Sections (specialized symposia and contributed papers).
6. The programs of the national meetings of the American Astronomical Society, American Society of Criminology, American Nature Study Society, American Society of Naturalists, American Society of Zoologists, Beta Beta Beta Biological Society, Biometric Society (WNAR), National Association of Biology Teachers, Scientific Research Society of America, Society for General Systems Research, Society of Protozoologists, Society of Systematic Zoology, and the Society of the Sigma Xi.
7. The multi-sessioned special programs of the American Association of Clinical Chemists, American Astronautical Society, American Meteorological Society, American Physiological Society, American Psychiatric Association, Association of American Geographers, Ecological Society of America, National Science Teachers Association, National Speleological Society—and still others, a total of some 70 to 80 participating organizations.
8. The sessions of the Academy Conference, the Conference on Scientific Communication, and the Conference on Scientific Manpower.
9. The sessions of the AAAS Cooperative Committee on the Teaching of Science and Mathematics, of the AAAS Committee on Science in the Promotion of Human Welfare, and of the Committee on Public Understanding of Science.
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